Minimization and Management of Wastes from Biomedical Research

Edward H. Rau,[1] Robert J. Alaimo,[2] Peter C. Ashbrook,[3] Sean M. Austin,[4] Noah Borenstein,[5] Michelle R. Evans,[6] Helen M. French,[7] Richard W. Gilpin,[8] Joseph Hughes Jr.,[9] Sherilynn J. Hummel,[10] Alice P. Jacobsohn,[11] Charlyn Y. Lee,[1] Scott Merkle,[12] Tad Radzinski,[5] Richard Sloane,[13] Kathryn D. Wagner,[14] and Larry E. Weaner[15]

[1]Environmental Protection Branch, Division of Safety, Office of Research Services, National Institutes of Health, Bethesda, Maryland, USA; [2]Procter & Gamble Pharmaceuticals, Norwich, New York, USA; [3]University of Missouri, Columbia, Missouri, USA; [4]Radiation Safety Branch, Division of Safety, Office of Research Services, National Institutes of Health, Bethesda, Maryland, USA; [5]U.S. Environmental Protection Agency, Region III, Philadelphia, Pennsylvania, USA; [6]Clinical Center, National Institutes of Health, Bethesda, Maryland, USA; [7]MERCI Program, Health Science Center Operating Room, University of Virginia, Charlottesville, Virginia, USA; [8]Johns Hopkins University and University of Maryland, Baltimore, Maryland, USA; [9]Worker Education and Training Program, Division of Extramural Research and Training, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA; [10]Burgess, Virginia, USA; [11]Environmental Industry Associations, Washington, DC, USA; [12]Safety and Health Branch, Office of Management, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA; [13]Laboratory of Toxicology, Division of Intramural Research, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA; [14]PRIZIM Inc., Olde Towne Gaithersburg, Maryland, USA; [15]The R.W. Johnson Pharmaceutical Research Institute, Spring House, Pennsylvania, USA

Several committees were established by the National Association of Physicians for the Environment to investigate and report on various topics at the National Leadership Conference on Biomedical Research and the Environment held at the 1–2 November 1999 at the National Institutes of Health in Bethesda, Maryland. This is the report of the Committee on Minimization and Management of Wastes from Biomedical Research. Biomedical research facilities contribute a small fraction of the total amount of wastes generated in the United States, and the rate of generation appears to be decreasing. Significant reductions in generation of hazardous, radioactive, and mixed wastes have recently been reported, even at facilities with rapidly expanding research programs. Changes in the focus of research, improvements in laboratory techniques, and greater emphasis on waste minimization (volume and toxicity reduction) explain the declining trend in generation. The potential for uncontrolled releases of wastes from biomedical research facilities and adverse impacts on the general environment from these wastes appears to be low. Wastes are subject to numerous regulatory requirements and are contained and managed in a manner protective of the environment. Most biohazardous agents, chemicals, and radionuclides that find significant use in research are not likely to be persistent, bioaccumulative, or toxic if they are released. Today, the primary motivations for the ongoing efforts by facilities to improve minimization and management of wastes are regulatory compliance and avoidance of the high disposal costs and liabilities associated with generation of regulated wastes. The committee concluded that there was no evidence suggesting that the anticipated increases in biomedical research will significantly increase generation of hazardous wastes or have adverse impacts on the general environment. This conclusion assumes the positive, countervailing trends of enhanced pollution prevention efforts by facilities and reductions in waste generation resulting from improvements in research methods will continue. *Key words*: biohazardous waste, biomedical research facilities, chemical waste, drug waste, hazardous waste, laboratories, medical waste, minimization, mixed waste, multihazardous waste, pollution prevention, radioactive waste, recycling, solid waste, training, waste disposal. — *Environ Health Perspect* 108(suppl 6):953–977 (2000).
http://ehpnet1.niehs.nih.gov/docs/2000/suppl-6/953-977rau/abstract.html

Introduction

Several committees were established by the National Association of Physicians for the Environment (NAPE) to investigate and report on various topics at the National Leadership Conference on Biomedical Research and the Environment held 1–2 November 1999 at the National Institutes of Health (NIH) in Bethesda, Maryland. This is the report of the Committee on Minimization and Management of Wastes from Biomedical Research.

Background

Waste management issues were among the core concerns addressed by the conference. It is anticipated that the budget of NIH will double in the next 5 years, and similar increases in for-profit research are expected. John E. Porter, Chairman of the House Subcommittee on Labor, Health and Human Services, and Education Appropriations, the conveners of the conference, and others have raised concerns that the boom in research activities associated with this funding will have the potential to increase generation of wastes that can be very damaging to the environment (*1*,*2*). The charge of the committee on Minimization and Management of Wastes from Biomedical Research was to address these concerns.

Committee Topics, Organization, Objectives, and Methods

Topics investigated. The scope of work assigned to the committee described in the conference agenda (*3*) was extensive. Major tasks included the following: characterization of the various types of wastes generated by biomedical research facilities; review of current waste management methods; evaluation of the potential for adverse impacts from waste generation on both the environment and the research mission; reporting on strategies for reducing these impacts; and providing examples of best practices for pollution prevention (source reduction or waste avoidance) and waste minimization (volume and toxicity reduction) at research facilities

Committee composition and organization. The chairman of the committee was appointed by NAPE. The committee comprised seven subcommittees, each with a chairperson appointed by the committee chairman. Six subcommittees focused on the various types of wastes generated by research facilities (biohazardous and regulated medical wastes, chemical wastes, pharmaceutical wastes, radioactive wastes, multihazardous

This article is based on a presentation at the Leadership Conference: Biomedical Research and the Environment held 1–2 November 1999 in Bethesda, Maryland, USA.

Address correspondence to E.H. Rau, NIH, 13 South Dr., MSC 5746, Bethesda, MD 20892-5746 USA. Telephone: (301) 496-7990. Fax: (301) 480-8056. E-mail: edrau@helix.nih.gov

The views expressed by the authors are their own and do not necessarily represent the official position of their respective organizations, agencies, or institutions.

We gratefully acknowledge the assistance of the National Association of Physicians for the Environment and the many individuals and organizations that contributed to this work. P. Hagen of Georgetown University in Washington, DC, served as co-chair of this committee and moderated the workshop session.

Received 3 May 2000; accepted 1 September 2000.

wastes, and solid wastes and recycling), and one subcommittee was assigned to review training issues relating to waste management. Subcommittee chairs were responsible for collecting information, presenting conference workshops, and preparing sections of this report applicable to their subject area.

Conference registrants who expressed an interest in waste issues were invited to serve on the committee, and additional members were recruited by the subcommittee chairs. Members were affiliated with a diverse spectrum of organizations, including academia, professional societies, pharmaceutical research laboratories, waste management industry, environmental organizations, NIH, U.S. Environmental Protection Agency (EPA), and state environmental agencies. All chairs and members served as unpaid volunteers, and no funds were received in support of the committee.

Sources of information and methods. The information in this report was compiled by the committee chairman and based largely on data provided by the members of the committee, published references, and input from attendees at the conference. Drafts of all subcommittee reports and the final, full report were distributed to the members for review. This report should be considered the consensus findings of the committee.

Characterization of Wastes from Biomedical Research

General categories of wastes. Biomedical research facilities generate a complex array of wastes, which may be broadly grouped into two categories: biomedical research wastes (BRW) that are direct products of research activities, and other conventional wastes from research support operations such as facility construction, operation, maintenance, and demolition, food service, and administrative functions.

With some exceptions, conventional wastes from biomedical research facilities are similar to or indistinguishable from wastes generated by other sources. Minimization strategies for these wastes and the issues surrounding their recycling and management are well established in the literature and are not covered in detail here. This report focuses on BRW. However, a boom in construction of new and renovated facilities will undoubtedly follow the anticipated increases in public and private funding for research. This has the potential to concomitantly increase generation of conventional wastes, especially construction and demolition wastes. These wastes must be appropriately managed and recycled or disposed of in a manner protective of the environment.

Characteristics of wastes from biomedical research. Major sources of BRW are laboratories, patient diagnosis and treatment, and husbandry of laboratory animals. These wastes, especially those from laboratory activities, may differ from wastes from other sources in several respects, and these differences may significantly affect how BRW is classified, regulated, and disposed.

Manufacturing facilities and most other large industrial operations tend to generate wastes that are few in number, recurring, and in relatively large volumes. This contrasts with biomedical facilities, which typically generate hundreds, sometimes thousands of different wastes, usually in small volumes, and often as the result of a one-time experiment or protocol. These properties significantly increase the complexity of BRW management and reduce the economies of scale. Unit costs of analyzing, processing, record keeping, shipping, treating, and disposing of BRW may be orders of magnitude higher than for conventional wastes.

Biomedical research wastes may contain multiple types of hazardous materials—combinations of toxic chemicals, radioactive materials, and biohazardous agents. Selecting treatment methods for these multihazardous wastes and determining the most appropriate sequence of treatment procedures is often a complicated and problematic task. The presence of multiple types of hazardous materials may also reduce or eliminate access to disposal facilities, as these facilities can usually process only a single type of waste.

The hazardous properties of many materials used in research may not be known or are described incompletely.

Biomedical research wastes, particularly those from medical procedures, may have aesthetically objectionable characteristics affecting how they must be managed. For example, pathological wastes may have to be processed in a manner that renders them unrecognizable before they are disposed.

Special security requirements may apply to handling and destruction of wastes that contain confidential or protected information and items that must be protected from diversion to unauthorized uses. Examples of such wastes include *a*) medical records, clinical specimens, and other items labeled with patient identification information; *b*) research data and samples; and *c*) controlled substances.

Quantities of wastes generated by biomedical research. Current and well-documented data on the amounts of wastes generated by biomedical research activities and national trends for these wastes are scant. There are no routine surveys or national reporting requirements for wastes except for certain hazardous wastes regulated by EPA. Hazardous waste-generation data must be reported by facilities on a biannual basis (*4*). Even for these wastes, it is difficult to determine the amount generated by biomedical research activities. Generation data from generator reports are aggregated by standard industry classification (SIC) codes. There is no applicable SIC code for facilities that only conduct biomedical research. At other facilities, such as hospitals and universities that have applicable codes, research wastes are mingled with wastes from nonresearch sources. Finally, many research activities are not conducted in facilities; they occur in clinics, doctors' offices, and homes. For example, investigational drugs or experimental devices may be given to patients for use at home. Wastes from these activities are disposed of by patients and others at off-site locations and are not reported by the originating research facility.

Although data are limited, it is possible to estimate the magnitude of contributions from biomedical research to the total amounts of various types of regulated BRW generated in the United States. Most research activities are conducted in laboratories, hospitals, and academic institutions, and some waste generation survey data are available for these types of generators. Although biomedical research accounts for a small fraction of the aggregate amounts of wastes reported by these generators, the data can be used to develop upper estimates for various types of BRW.

Hazardous wastes. A survey conducted in the late 1980s reported that less than 1% of the hazardous wastes generated annually in the United States came from the 30,000 educational institutions in existence at the time (*5*). All laboratories combined, regardless of function, generated less than 1/100 of 1% of the nation's hazardous waste (*6*).

Medical wastes. Laboratories contribute 3.3% and hospitals 77.1% of the total amount of regulated medical wastes in the United States (*7*). There are no reliable data on medical waste generation from nonhospital health care sites (*8*).

Radioactive wastes. Medical and research facilities combined account for less than 5% of the total volume of low-level radioactive wastes generated in the United States (*9*).

Multihazardous wastes. Data are not available on generation of multihazardous wastes except for regulated mixed wastes (radioactive hazardous wastes). A national survey of generators of mixed waste reported that medical facilities accounted for 564 m^3, or 20.4%, of the total reported generation of 2,765 m^3 (*10*).

From this limited information it is apparent that biomedical research facilities account for a very small to negligible fraction of the total amounts of regulated wastes generated in the United States. It should be understood that the potential impacts of these wastes are only partially determined by the amounts of waste generated. The concentrations and

environmental toxicology of hazardous constituents in the waste, and the protectiveness of methods used to treat and dispose of the wastes may be larger determinants of potential risks to the environment. These factors are reviewed later in this report.

Incentives for Improving Waste Minimization and Management

There are strong incentives for improving waste minimization and management programs in research facilities.

Reduction of institutional health and safety hazards. The potential for exposures of employees, patients, visitors, and waste management personnel to safety, fire, and health hazards associated with wastes is reduced. Greater emphasis on source reduction (waste avoidance) practices eliminates or reduces waste generation and its hazards. Other minimization practices reduce the volume and toxicity of unavoidable wastes, and improvements in transportation, storage, treatment, and disposal of wastes reduce hazards by ensuring containment of hazardous materials and prompt removal of these materials from the workplace.

Environmental protection. Wastes and pollutants from research activities can directly cause damage to the environment if released in an uncontrolled manner or treated improperly before disposal, or if treated wastes are discharged into inappropriate environmental media. Even if wastes are managed properly, secondary wastes and pollutants from their transportation, recycling, and treatment are an inevitable consequence of waste generation. These impacts can only be prevented by elimination of wastes at the source—pollution prevention.

Regulatory compliance. Disposal of hazardous, radioactive, and medical wastes is an intensely regulated activity. A complex framework of Federal, state, regional, and local laws, licenses, and permits govern virtually all aspects of waste management from "cradle to grave," including labeling and identification, on-site storage and management, transportation, treatment, and disposal. Severe penalties may be levied against both facilities and individuals for noncompliance. These may include criminal or civil actions leading to restrictions or revocations of facility operating permits, fines, and imprisonment. Academic and research facilities have recently been the focus of enhanced enforcement efforts by EPA and state agencies (*11,12*).

Laws providing general mandates for pollution prevention and waste minimization have also been enacted. These include the Solid Waste Management Act of 1965 (*13*), as amended by the Resource Conservation and Recovery Act of 1976 (RCRA) (*14*), and the Pollution Prevention Act of 1990 (*15*) (PPA). Enabling Federal regulations setting forth specific source reduction and minimization requirements have not been established for most types of wastes. RCRA regulations requiring generators to reduce the volume and toxicity of hazardous (chemical) wastes is the major exception. Biomedical research programs conducted by Federal agencies are also subject to several Executive orders requiring agencies to establish pollution prevention programs, set waste reduction goals, and use products made from recycled materials. The most comprehensive of these is Executive Order 13148 of April 21, 2000, titled *Greening the Government Through Environmental Leadership* (*16*).

Liability avoidance. Significant short-term and long-term liability is associated with generation of all types of wastes, particularly hazardous and radioactive wastes. Liability for costs relating to remediation of environmental damage from these wastes (environmental impairment liability) may be catastrophic. Generators never escape liability for their wastes. Even if wastes are managed and disposed of in accordance with all regulatory requirements by fully licensed and permitted contractors, the generator retains liability and may be responsible for damages found years later. Liability is also joint and several. Generators responsible for a relativity small amount of waste at a contaminated site may incur liability for clean up of a disproportionately large fraction of the total costs.

Disposal cost avoidance. Costs associated with management and disposal of wastes may consume a significant amount of research funds. For many facilities, avoidance of these costs provides ample justification for implementation of comprehensive source reduction and minimization programs. Unit costs for disposal of BRW are often much higher than for conventional wastes, and these costs may differ by orders of magnitude among the various types of wastes. Typical treatment and disposal costs have not been published. Examples of estimated unit costs reported to the committee by NIH and other committee members are presented in Table 1 to illustrate the magnitude of costs that may be encountered and differences among different types of wastes. (Actual costs incurred by other facilities may vary considerably from these estimates and will be affected by many factors such as concentrations of hazardous constituents in the waste, management methods, volume of waste, contractors and disposal facilities used, and location of the research facility).

Community relations. Waste management issues are a major source of public concern. Misinformation on waste management can create misperceptions about research facility operations. Facilities with open, well-managed pollution prevention and waste management programs help to maintain public confidence in the research program.

Value of laboratory wastes as a teaching tool. Although the amounts of wastes and pollutants generated by individual research procedures are usually small, they provide an excellent opportunity for investigators to learn, practice, and teach the principles of environmental stewardship in the laboratory. These lessons can then be applied to ensure that the products of biomedical research and development—medical procedures, drugs, and supplies—will not become major sources of pollution and wastes, as they are subsequently used on a large scale in the health care system.

General Strategies for Pollution Prevention and Waste Minimization

The PPA established as a national policy a hierarchy of waste minimization and management approaches with preference for those providing the greatest protection of the environment:

> The Congress hereby declares it to be the national policy of the United States that pollution should be prevented or reduced at the source whenever feasible; pollution that cannot be prevented should be recycled in an environmentally safe manner whenever feasible; pollution that cannot be prevented or recycled should be treated in an environmentally safe manner whenever feasible; and disposal or other release into the environment should be employed only as a last resort and should be conducted in an environmentally safe manner. (*15*)

The PPA provides guidance for selecting general approaches to pollution prevention and waste minimization solely on the basis of environmental considerations. For research facilities, it is of paramount importance to ensure that the approaches used will not have adverse effects on patients, laboratory

Table 1. Typical unit costs for treatment and disposal of various types of wastes generated by biomedical research facilities.

Type of waste	Unit cost (U.S. dollars)[a]	Units
Solid wastes, nonhazardous	0.10	kg
Medical wastes, regulated	1.00	kg
Bulk solvents, drum lots	0.50–1.50	L
Liquid scintillation counting vials	1.70–2.50	kg
Chemicals shipped in lab packs	9.00–30.00	kg
Chemicals, highly reactive	25.00–> 350.00	kg
Low-level radioactive wastes, solid	20.00–50.00	kg
Animal carcasses, radioactive	35.00–50.00	kg
Low-level radioactive mixed wastes, liquid	5.00–> 250.00	kg
High-^{3}H mixed wastes, liquid	8,000,000–33,000,000	L

[a]These are only costs of waste treatment and disposal; other costs associated with waste collection, analysis, accounting, packaging, storage, processing, and shipping are not included.

animals, and scientific productivity. Cost effectiveness and feasibility should also be considered. With these considerations in mind, many facilities have found that many of the same pollution prevention and waste minimization strategies used in industry can be successfully applied to research operations. These strategies include *a*) better procurement management, especially avoiding overordering of hazardous materials; *b*) substitution of hazardous materials with less hazardous or nonhazardous materials; *c*) reducing the scale of experiments and protocols to the minimum size necessary to achieve research objectives; *d*) redistribution, reuse, and recycling of supplies and reagents; and *e*) improved waste segregation to maximize recovery of materials and treatability of wastes; and *f*) ensuring that all staff members are aware of the need to minimize wastes and are trained on minimization methods applicable to job duties.

Ultimately, the best ideas for pollution prevention often originate from within the research community itself. Investigators are intimately familiar with the research procedures and objectives of experimental protocols and can evaluate the trade-offs associated with changes in procedures necessary to achieve pollution prevention objectives. Increasing the awareness of researchers of the problems associated with management of BRW is the first step. The innovations in research methods that follow can have a long-lasting effect on laboratory operations and the quantity of wastes generated from these activities.

The EPA Waste Minimization Opportunity Assessment Manual (*17*) provides further guidance on selecting waste minimization methods. Other comprehensive references on waste minimization and management with emphasis on laboratories and medical facilities are available (*18–21*). Examples of best practices for waste minimization and management in biomedical research facilities are presented in the subcommittee reports that follow.

Subcommittee Reports

Subcommittee on Biohazardous and Regulated Medical Wastes

Classification and Definitions

Research facilities often generate significant quantities of wastes containing materials of biological origin. These biological wastes may be subject to special management requirements under Federal, state, or local regulations if they contain, are contaminated with, or perceived to be contaminated with *a*) biohazardous (infectious) agents; *b*) blood or other body fluids; *c*) toxins; *d*) pathological wastes—solid human or animal tissues; *e*) genetically altered materials or organisms; and *f*) needles, scalpels, syringes, and other sharp objects that present physical hazards and may be contaminated with biohazardous agents. Biological wastes subject to these requirements are referred to in this report as regulated medical wastes (RMW).

Because biohazardous waste is regulated by various agencies and accrediting organizations with different authorities, policies, and concerns, there is not a singular method by which biomedical research facilities can define it. Biohazardous waste is usually considered by the scientific community to be a waste that could, in a susceptible host, cause infection that may develop into a disease—a recognizable departure from normal. However, the public often perceives a waste to be biohazardous on the basis of its source and appearance. Waste appearing to originate from a hospital, clinic, or biomedical research laboratory is often assumed biohazardous, even if, scientifically, potentially infectious microorganisms or toxins are not present.

The regulated community is often frustrated by the lack of consistency in definitions of RMW. Several attempts have been made to create a definition that can be used by all interested parties. The most recent of these was described in a U.S. Department of Transportation (DOT) advance notice of proposed rulemaking (*22*). Here DOT proposed to define infectious substances (and wastes) on the basis of risk groups (RGs) of the World Health Organization (WHO). These RGs characterize infectious substances on the basis of the pathogenicity of the organism, mode and relative ease of disease transmission, risk of infection to individuals and community, and reversibility of the disease through known and effective preventative agents and treatment.

To ensure proper characterization and management of RMW, research facilities should review Federal, state, and local regulations for current definitions and requirements. See Wagner (*23*) for a more complete discussion of RMW definitions and related issues.

Characterization of RMW from Biomedical Research

The composition of RMW generated by biomedical research facilities is generally similar to that generated by hospitals and other healthcare installations. However, wastes from some research facilities may contain additional constituents not commonly found in wastes from healthcare.

Carcasses, bedding, and other wastes from the care and use of laboratory animals. Carcasses are usually incinerated even if they are not biohazardous or regulated as RMW.

Genetically altered materials and organisms. These are usually managed in the same manner as RMW. The recommended inactivation and disposal methods vary depending on the biosafety level assigned to each material (*24*).

Other hazardous contaminants (chemicals, drugs, and radioactive materials). If these are present, the wastes must be managed as multihazardous wastes.

The amount of RMW generated by biomedical research activities depends on several factors, including the nature of the research, the type and size of the facility, waste definitions used, and the effectiveness of minimization efforts. Typical biomedical research laboratories usually generate up to 20 kg of biohazardous wastes per day; a clinical microbiology laboratory may generate hundreds of kilograms. A large, thousand bed, tertiary care hospital may generate up to 6 tons of biohazardous waste per day.

Assessment of Potential Environmental Impacts

Direct impacts—biohazards. After extensive studies conducted under provisions of the Medical Waste Tracking Act of 1988 (*25*), EPA concluded that the disease-causing potential of medical waste is greatest at the point of generation and naturally tapers off after that point, thus presenting more of an occupational concern than a generalized environmental concern. Risk to the public of disease caused by exposure to medical waste is likely to be much lower than risk for the occupationally exposed individual (*26*). There is no scientific evidence of disease transmission from medical wastes via environmental media (*8,27*). Several factors limit the potential for disease transmission from biomedical research facility wastes:

Most facilities do not handle high-risk organisms. The Centers for Disease Control and Prevention and NIH classify infectious agents and laboratory activities involving manipulation of biohazardous agents into four biosafety levels (BSLs) (*28*). The BSLs range from 1 to 4, with BSL 1 representing the agents that pose the lowest risk of disease transmission. This classification system is widely accepted by regulatory bodies in the United States, although recent debate at the Federal level opened the door to using the RGs of the WHO. The WHO RGs also range from 1 to 4. RG 1 represents microorganisms that are unlikely to cause human or animal disease. RG 4 is used for pathogens that usually cause serious disease that can be readily transmitted and for which effective treatment and preventative measures are not usually available. Regardless of which risk-based system is used, few biomedical research facilities handle agents more hazardous than

those typically found in medical wastes from hospitals and other healthcare facilities (BSLs 1 and 2; RGs 1 and 2). Research with agents classified as BSLs 2, 3, and 4 (RG 2, 3, and 4) is performed only in facilities designed, operated, and permitted in a manner that assures containment of the agents. Guidance on the design and operation of infectious waste management systems for such facilities is available (*29*).

Cultures are inactivated before disposal. Biohazardous waste with the greatest potential for causing disease in a susceptible host is waste that contains cultures of pathogenic microorganisms. Although other biohazardous forms of RMW may transmit disease, the risk is considerably less. Microbiologists generally decontaminate cultures of microorganisms before discarding the treated material into the RMW stream. Operational guidelines strongly recommend all wastes from BSLs 2, 3, and 4 be inactivated before they are disposed (*28*).

Concentrations of potentially infectious agents in RMW are relatively low. The concentrations of human pathogens in medical waste are lower than those in household wastes, and these wastes pose nominal risks (*30,31*).

Infectious agents routinely encountered in RMW are not resilient under environmental conditions. Many human pathogens found in medical waste tend to inactivate rapidly when released into the general environment, and conditions in landfills do not favor their growth or survival (*31*).

Indirect impacts from waste treatment operations. Incineration and other medical waste treatment processes can generate secondary wastes and pollutants if treatment facilities are not designed, constructed, and operated properly. These pollutants may have adverse environmental impacts.

Air emissions. Polychlorinated dioxins and dibenzofurans, toxic heavy metals (mercury and cadmium), and corrosive gases (hydrogen chloride) may be produced by medical waste incinerators (*32*). Varying levels of pollutants may also be emitted from alternative (nonincineration) treatment processes, depending on the method used for pathogen inactivation and the type of waste being treated. Whether these pollutants are released into the environment or contained depends on a number of operational factors and the level of technological advancement inherent in the treatment system.

Wastewater effluents. Another potential source of indirect impacts is the use of chemical disinfectants that may be regulated as toxic pollutants under the Federal Water Pollution Control Act (Clean Water Act) (*33*), and state and local pollution control laws. Phenolic disinfectants are of particular concern because they may disrupt wastewater treatment processes or result in discharges of toxic effluents. Many publicly owned treatment works (POTWs) have set allowable wastewater concentration limits for phenolic compounds at very low levels, precluding disposal of wastes containing these disinfectants via the sewerage system.

Planning for Improved RMW Source Reduction and Management Strategies

Disposal of RMW continues to be a costly component of healthcare and biomedical research. Consequently, many facilities have developed comprehensive plans for source reduction and improved management of medical wastes. Designing such a plan requires a multidisciplinary team. The team must be capable of *a*) conducting an environmental, health, and safety audit; *b*) using survey methods to collect baseline data on the quantities and types of waste generated by the facility; *c*) developing and implementing a system to both identify source reduction action items and track progress; and *d*) ensuring staff training. To be cost effective, the extent of the program must be tailored to fit the size of the facility and the total amount of waste generated (*34,35*).

Early involvement of employees in the planning process and continuous training of employees are critical elements of successful medical waste minimization programs. Employees must be fully aware of the contents of the facility's waste management plan, including regulations that apply, how to segregate the types of waste the facility generates, how to choose environmentally preferable materials, and how to properly dispose of unavoidable wastes. There also should be a feedback system such that a facility can detect, investigate, and correct deficiencies and problems with the plan itself.

Source Reduction Methods

Improved segregation of wastes. Improving segregation of wastes is probably the strategy most widely and successfully used by healthcare institutions to reduce generation of RMW. The application of this strategy in research facilities is feasible but sometimes more difficult.

Segregation is easiest to implement in areas where waste streams are recurring and well characterized. This is not the situation in research facilities, where unique, small-quantity waste streams are often generated from one-time experiments or special projects. Despite this difficulty, separating medical waste streams into infectious/noninfectious waste or regulated/nonregulated categories should be possible. If large amounts of waste are generated, additional segregation of wastes treated on-site from those shipped off-site may greatly diminish facility expenses.

Compliance with segregation requirements is improved by placing containers of the appropriate size and type in convenient locations. In biomedical facilities, the large number of potential segregation categories, limited space availability for collection containers, and logistical problems associated with collecting many small waste streams may limit this practice.

Other methods. Many other source reduction methods have been successfully used by healthcare facilities to reduce generation of medical wastes; these may be applicable to biomedical research facilities as well. Examples include *a*) reprocessing and reuse of disposable medical supplies (*36*); *b*) use or donation of unused or reprocessed medical supplies (*37,38*); *c*) reduced use of disposables and elimination of excess packaging; and *d*) use of dissolvable gowns and other medical supplies (*39*).

Some plastics and other materials in biohazardous waste may be recycled in a cost-effective and environmentally protective manner. The level of recycling for biohazardous wastes is not fully known but is probably low. Recycling options are limited by factors such as regulatory restrictions, concerns over the efficacy of treatment for infectious agents that may have contaminated the material to be recycled, quality control issues, public perceptions, and the limited markets for materials recovered from these wastes. Costs associated with sorting recyclable materials and shipping and processing them for recovery further impact the cost effectiveness of recycling.

Trends in research methodology also affect the reuse and recycling of decontaminated wastes from research laboratories. For example, up until the 1950s, bacteriologists used reusable glass petri dishes. They then switched to disposable plastics. Likewise, in the late 1970s, microbiologists switched to using plastic pipettes instead of glass. The use of glass in the laboratory is not likely to change because of the labor costs involved with cleaning and sterilizing. Impurities in glass can also interfere with sensitive molecular biology techniques. In addition, the wastewater produced from the cleaning and sanitizing process is an environmental tradeoff to reduced waste disposal.

Management of Unavoidable Medical Wastes

Generation of RMW from most biomedical research facilities is unavoidable. This waste must be collected, treated, and disposed of in a manner that is safe, cost effective, and protective of the environment.

The primary objective of RMW treatment is inactivation—reducing the concentration of pathogens in the waste to levels not

hazardous to public health and safety. Secondary objectives may include *a*) encapsulation or destruction of sharps; *b*) preventing or retarding putrefaction and generation of odors; *c*) physical alteration to remove aesthetically objectionable characteristics, destroy confidential patient or research information, or render discarded materials unrecognizable as medical waste; *d*) volume reduction; and *e*) stabilization of treated wastes to minimize potential impacts on the environment from final disposal.

Currently, over 90% of medical wastes is treated by incineration (*26*). However, recent rulings (*40*) under the Clean Air Act (*41*) and the Clean Air Act Amendments (*42*) are forcing change. Under these new rules, existing incinerators face costly retrofitting or possible closure in favor of newer incinerators capable of complying with the new standards. EPA anticipates that many older, hospital-based units will shut down within the next three years and newer off-site, commercial units will be used at full capacity.

Reductions in the use of on-site incinerators and costs associated with shipping and disposal at commercial facilities are also encouraging rapid development and greater use of alternate (nonincineration) treatment technologies for solid medical wastes. These include systems using chemical disinfectants, low-pressure steam sterilization (autoclaves), high-pressure steam (steam reforming), microwaves, radiation, plasma arc pyrolysis, alkaline hydrolysis (tissues and animal carcasses), and other specialized methods for narrowly classified waste streams. Usually, some combination of technology options must be used, because most alternate technologies cannot be used to process all of the various types of RMW generated by biomedical research facilities. For example, autoclaves are not suitable for treating waste that contains chemotherapeutic drugs, and only a few autoclave systems are approved for the treatment and destruction of pathological wastes.

Many manufacturers provide alternative treatment systems, and disposal services using some of the technologies are now commercially available. Each of these technologies has specific strengths and weaknesses that must be carefully examined and matched with the unique needs, waste streams, priorities, and circumstances of each generator. Guidance on evaluating and selecting treatment and disposal methods for RMW may be found in references listed on the EPA Medical Waste Home Page (*43*) and reviews (*44,45*).

Current Issues Affecting Management of RMW

Uniform definitions and regulations for management of RMW are needed. The varying definitions of RMW and requirements for its management imposed by different Federal agencies, states, and local governments can cause confusion and add unnecessary costs to managing RMW. This is particularly evident when RMW must be shipped through multiple jurisdictions to distant commercial facilities for processing and disposal.

Some definitions of RMW are too broad, and regulations may require excessive treatment. Under some waste regulations, the mere presence of materials from a biomedical laboratory causes the waste to be considered biohazardous and subject to regulation as medical waste. Other regulations require treatment steps not necessary to reduce risk. For example, the Maryland statute uses the "reasonable person perception rule" to define medical waste. "Special medical waste," a Maryland term used for RMW, must be treated and rendered nonrecognizable before it can be landfilled (*46*). Other states permit recognizable, autoclave-treated biohazardous waste to be landfilled. Overregulation of medical waste management increases costs and imposes treatment requirements such as incineration, which may more adversely effect the environment than burial of untreated waste.

The inclusion of criteria such as appearance or waste origin in definitions of RMW also complicates management of multihazardous wastes and may restrict access to appropriate disposal facilities. Research procedures frequently generate wastes with multiple hazardous properties (see section "Subcommittee on Multihazardous Waste"). An appropriate method to manage multihazardous wastes with biohazardous properties is to first inactivate the pathogens that may be present. The inactivated wastes can then be shipped to facilities that have the appropriate technologies for treatment and disposal of the remaining hazardous constituents (hazardous chemicals or radioactive materials). This may not be feasible if the inactivated waste retains its legal classification as RMW. Most hazardous and radioactive waste disposal facilities do not accept RMW because they do not have the requisite permits or capability to handle medical wastes.

Evaluation criteria for alternate technologies should consider other contaminants typically present in RMW. Criteria for evaluation of alternative medical waste treatment technologies are available (*47*). However, these address only the effectiveness of the process in inactivating pathogens. Medical wastes frequently contain residues of antineoplastic agents, drugs, and other hazardous, nonbiological contaminants. Evaluation criteria should be revised to include tests to determine the effectiveness of the technology in treating these contaminants.

Conventional inactivation procedures may be inadequate for inactivation of wastes containing agents of transmissible degenerative encephalopathy. Transmissible degenerative encephalopathies (TDEs) such as scrapie and Creutzfeldt-Jakob disease are the subject of numerous research studies in progress. Standard autoclaving, chemical disinfection, and gas sterilization procedures effective for inactivation of all previously known types of pathogens may not be effective for inactivating the prior agents that cause TDE. These agents are highly resistant to inactivation, and accidental transmission has occurred with inadequate decontamination procedures. A recent study suggests that these agents may even survive exposure to temperatures reached during incineration of medical waste (*48*). Standard inactivation methods should be modified for treatment of wastes that may be contaminated or potentially contaminated with agents of TDE (*49–51*).

Management of medical wastes generated outside facilities. Much of the medical waste associated with biomedical research is generated by patients and healthcare providers in homes and other areas outside facilities. Research programs should provide guidance to all participants on how medical wastes should be managed. Guidance documents on disposal of medical wastes from home healthcare are available (*52–54*).

Examples of Best Practices

Source reduction program at a major hospital. The New York Hospital in Queens, New York, set a goal for its waste management plan to conserve natural resources, minimize the hospital's impact on the community's resources, and refocus funding from waste disposal to patient care. First, the hospital created a "Green Team" to encompass all levels of the organization, including the board of trustees, the chairman, administration, nutrition services, nursing, building services, quality management, materials management, and human resources. The team's mission was to reeducate the entire facility concerning waste reduction and conservation through phased projects. The first phase focused on medical waste. The team conducted a survey and found that items such as paper towels, pizza boxes, intravenous (iv) tubing, and iv solution bags were all being placed in red bags as RMW. With this information, the team made changes in the placement of waste containers such that sorting of medical waste became easier. The team then provided inservice training to educate staff about proper disposal. After initial implementation, the team established a schedule for periodic unannounced waste surveys. On the basis of the surveys, the staff was reeducated until they reached full compliance. The effort reduced the volume of RMW disposal by 71%.

Clearinghouse for source reduction information. Numerous additional examples of best practices and case studies relating to reduction of medical wastes and obtained online from the EPA Waste Reduction Resource Center (*55*), using the center's P2 Info House information retrieval function and entering the search term "medical waste."

Development of alternate technologies by biomedical research facilities. Some biomedical facilities have been active in research and development of alternate technologies for treatment and disposal of RMW. An example is the Biosafety Division of the Department of Health, Safety and Environment, at Johns Hopkins in Baltimore, Maryland, which has been investigating for 8 years various alternate technologies to replace medical waste incineration. Examples of technologies investigated include grinding/microwave, grinding/microwave/grinding, chemical/grinding, autoclave/grinding, grinding/superheating, and autoclave/liquid/grinding. The outcome of this research was the successful development of superheated water and steam liquid grinding system that inactivates RMW and produces a product that is not recognizable as medical waste and is acceptable for direct disposal as nonbiohazardous municipal waste. The overall operating cost for the equipment, including labor, was nearly half the contract price to ship the waste to a regional medical waste incinerator (*56*).

Subcommittee on Chemical Wastes

This section presents information relating to management of chemical wastes (hazardous wastes). Pharmaceuticals are addressed in the section "Subcommittee on Pharmaceutical Wastes"; chemical wastes containing radioactive materials or biohazardous agents are addressed in the section "Subcommittee on Multihazardous Wastes."

Classification and Characterization of Chemical Wastes

Classification. Chemical wastes may be divided into the following groups: *a*) hazardous wastes regulated under RCRA (e.g., flammable solvents, acids, bases, toxic metals); *b*) special wastes regulated under other laws (e.g., polychlorinated biphenyls, used oil); *c*) nonregulated hazardous wastes (e.g., ethidium bromide, aflatoxin); *d*) chemically contaminated laboratory materials (e.g., papers, gloves, glassware); and *e*) nonhazardous chemical wastes (e.g., sugars, buffers).

Sources. As a broad generalization, biomedical research facilities produce smaller amounts and a larger variety of chemical wastes and mixtures than industry, which produces large amounts of a small number of chemical wastes. Because individual research laboratories tend to conduct unique research, large institutions can use a large number of different chemicals. For example, NIH has over 625,000 chemical compounds in use or in repositories. Most of these chemicals are in quantities of < 100 g. The regulated hazardous and special wastes produced by biomedical laboratories are primarily mixtures of organic solvents, with lesser amounts of other materials such as used oil, contaminated labware, and miscellaneous chemicals.

Activities that result in chemical wastes primarily include *a*) disposal of excess, outdated, and off-specification chemicals; *b*) molecular biology procedures (e.g., extraction, purification and sequencing of nucleic acids, proteins); *c*) analytical procedures (e.g., assays, gel electrophoresis); *d*) histological procedures (e.g., fixatives, stains); *e*) other experimental uses of chemicals; *f*) cleaning and disinfection; *g*) care and maintenance of laboratory animals; *h*) film processing; *i*) facility operations (e.g., paint, floor cleaners, floor strippers, batteries, fluorescent light tubes, and ballasts); and *j*) disposal of contaminated labware and spill clean-up residues. More detailed information of the hazardous substances produced by specific biomedical procedures is available (*57*–*59*).

Quantities generated. In analyzing potential economic impacts on various economic sectors prior to the adoption of the first RCRA regulations in 1980, EPA estimated that academic institutions—a group larger than biomedical laboratories—generated less than 1% of the nation's hazardous waste (*60*). There are no indications that this proportion has changed over the past 20 years.

Assessment of the Potential for Environmental Impacts from Chemicals in Wastes from Biomedical Research

Approach. The committee sought to develop a preliminary assessment of the risks posed to the environment from chemicals used in biomedical research facilities, and based on this assessment, determine which of the myriad chemicals in use should receive priority in planning minimization efforts. The assessment was performed by collecting data on chemicals present in hazardous wastes from research facilities and comparing the data with lists of chemicals that pose the greatest threat to the environment. The approach used in this assessment followed that established in the EPA Waste Minimization National Plan (*61*), and probably represents the first attempt to apply the methodologies recommended in the plan to BRW.

Persistent, bioaccumulative and toxic chemicals list. For this assessment, chemicals identified by EPA as persistent, bioaccumulative, and toxic (PBT) were assumed to pose the greatest potential threat to the environment. PBT chemicals do not break down or decrease in potency when released to the environment, even if released in very small, legally permitted quantities. Over time, these chemicals are likely to accumulate in soils or other environmental media. The chemicals can also be absorbed or ingested by plants and animals, accumulate in animal tissues to be passed through the food chain, and potentially cause long-term human health effects such as cancer or ecological problems. Several initiatives have been developed that place a focus on PBT chemicals identified by the Waste Minimization National Plan. The draft RCRA PBT List published in 1998 (*62*) was used in this assessment and consisted of 53 chemicals.

Collection of waste generation data. Waste generation data for this assessment were obtained from three facilities: the NIH main campus at Bethesda, Maryland (*63*), the National Institute of Environmental Health Sciences (NIEHS) campus at Research Triangle Park, North Carolina (*64*), and the R.W. Johnson Pharmaceutical Research Institute (RWJPRI) (*65*) at Spring House, Pennsylvania. These facilities were selected because all of their wastes are from biomedical research activities, and the facilities were representative of different types of research programs. Wastes generated in 1998 from approximately 4,000 laboratories, animal care facilities, and the NIH Clinical Center (CC), a major research hospital, are included in the NIH data. NIH waste accounting system allowed the estimation of net weights of specific chemicals in wastes by concentration-based calculations for every waste container received for disposal. Data for NIEHS were compiled from chemical name listings and gross weights in hazardous waste generation records from 1998; data from concentration-based calculations were not available. For NIH and NIEHS, a descending rank order listing of all hazardous chemicals generated in 1998 was produced. The top 100 chemicals (by total weight generated) for each facility were used for comparison with the list of PBTs. Quantitative data were not available from the RWJPRI; however, a representative of the facility was asked to compare the constituents typically present in their wastes with the NIEHS and NIH rank order listings and the PBT list and to report any significant differences in chemical use and disposal.

Results. The assessment was performed and reported by Borenstein and Radzinski (*66*). Results are summarized in Table 2. The characterization of PBTs in the wastes from the three facilities was similar and suggests that the chemicals present in wastes from research facilities present a low potential for adverse impacts on the environment:

- The top 100 chemical lists from NIH and NIEHS included 156 different chemicals. Of these, only 15 (~10%) are currently on the draft RCRA PBT list. Of the 156 compounds, 79 chemicals (51%) were not considered PBTs. The remaining chemicals were either not specifically evaluated or their PBT status could not be determined from the information presented. For instance, the elemental forms of some heavy metals are classified as PBTs. However, except for mercury and lead, their compounds are not. On the other hand, cyanides, and insoluble oxide/hydroxide forms are problematic and currently are classified as PBTs.
- The PBTs present in the wastes in the highest amounts were organic compounds, primarily chloroform and phenol. With the exception of these two compounds, the PBTs present in the wastes were minor constituents of the wastes from these facilities.
- With the exception of chromium, heavy metal PBTs are minor constituents of the hazardous waste streams from laboratories at all three facilities. Chromium compounds find limited use in certain staining procedures and in cleaning glassware. Significant quantities of lead, nickel, and cadmium, and small amounts of mercury were generated by the NIH and NIEHS facilities. These were components of discarded articles (batteries, shielding, and laboratory apparatus), which were shipped to recycling facilities for reclamation. Recycled metals were not included in rank order calculations.
- Some differences in the chemicals found in wastes and their rank order were noted among the three facilities, which probably reflect differences in their research focus. Wastes from NIH are primarily generated from molecular biology procedures (DNA and protein extraction, sequencing, and synthesis). NIEHS, although organizationally part of NIH, conducts research on environmental health and toxicology. The RWJPRI is involved in drug investigation and development activities. The notable differences between PBTs in wastes from the RWJPRI and the NIH facilities were the presence of nitrobenzene, which was not reported in wastes from NIH and NIEHS, and significantly lower levels of chloroform and phenol in the wastes from the RWJPRI.

The subcommittee concludes that potential chemical hazards from biomedical research wastes are probably of most significance to laboratory workers and secondarily to persons who might be accidentally exposed to small volumes of acutely hazardous wastes. Because relatively small amounts of hazardous chemicals are used in biomedical research, and most of these are not PBTs, chemicals in BRW present an insignificant hazard to the general environment. There are currently adequate numbers of commercial facilities available to handle virtually all hazardous wastes generated from biomedical research.

Table 2. Prevalence of persistent, bioaccumulative, and toxic chemicals[a] in hazardous wastes from three biomedical research facilities.

Chemical Abstracts Registry No.	Chemical name	Presence of chemical in facility wastes: NIH[b]	NIEHS[c]	Pharmaceutical research laboratory[d]
101553	4-Bromophenyl phenyl ether			
83329	Acenaphthene			
208968	Acenaphthylene			
120127	Anthracene			
7440360	Antimony[e,f]			
7440382	Arsenic[e]	•	•••	Yes
191242	Benzo(*g,h,i*)perylene			
7440417	Beryllium			
117817	Bis(2-ethyhexyl)phthalate			
85687	Butyl benzyl phthalate			
7440439	Cadmium[e,f]	•		Yes
67663	Chloroform	••••	••••	Yes
7440473	Chromium[e,f]	••	•••	Yes
7440508	Copper[e,f]	•		Yes
57125	Cyanide	•	••	Yes
84742	Dibutyl phthalate	•		Yes
95501	1,2-Dichlorobenzene			
541731	1,3-Dichlorobenzene			
106467	1,4-Dichlorobenzene			
75343	1,1-Dichloroethane	•		Yes
959988	Endosulfan, alpha			
33213659	Endosulfan, beta			
206440	Fluoranthene			
86737	Fluorene			
76448	Heptachlor			
1024573	Heptachlor epoxide			
118741	Hexachlorobenzene			
87683	Hexachlorobutadiene			
58899	Hexachlorocyclohexane, gamma			
7439921	Lead[e,f]	•	•	Yes
7439976	Mercury[e,f]	•	•	Yes
72435	Methoxychlor			
91576	2-Methylnaphthalene			
91203	Naphthalene	••		
7440020	Nickel[e,f]	•		Yes
98953	Nitrobenzene			Yes
29082744	Octachlorostyrene			
608935	Pentachlorobenzene			
82688	Pentachloronitrobenzene			
87865	Pentachlorophenol		•	
85018	Phenanthrene			
108952	Phenol	••••	••••	Yes
732263	Phenol, 2,4,6-tris(1,1-dimethylethyl)-			
None	Polychlorinated dibenzofurans			
None	Polychlorinated dibenzo-*p*-dioxins			
None	Polycyclic aromatic compounds			
129000	Pyrene			
7782492	Selenium[e]			Yes
95943	1,2,4,5-Tetrachlorobenzene			
120821	1,2,4-Trichlorobenzene			
71556	1,1,1-Trichloroethane			
95954	2,4,5-Trichlorophenol			
7440666	Zinc[e,f]	•		

Rank by total net weight in wastes from NIH and NIEHS facilities in 1998:
•••• Top 20 chemicals
••• Top 21–60 chemicals
•• Top 61–100 chemicals
• Not present in top 100 but greater than 1 kg (NIH) or 0.1 kg (NIEHS) disposed of per year

[a]Chemicals on the EPA Draft RCRA Waste Minimization PBT chemical list (*62*). [b]Based on combined data for all NIH facilities in Maryland and the District of Columbia excluding the Frederick Cancer Research and Development Facility at Frederick, Maryland (*63*). [c]Based on combined data for all NIEHS laboratories at Research Triangle Park, North Carolina, facility (*64*). [d]Based on nonquantitative data from R.W. Johnson Pharmaceutical Research Institute Laboratory (*65*). [e]Data include compounds of the listed element. [f]Does not include metal content of batteries, shielding, and other articles that are recycled and not disposed of as hazardous waste.

Planning for Chemical Waste Minimization

An effective hazardous waste minimization program requires careful planning and implementation. A great deal of information has been published on preparing a waste minimization program, but most such programs need to be customized to each facility. Programs should include waste characterization and accounting systems so trends can be evaluated and opportunities for waste minimization can be identified in planning, setting reduction goals, and tracking performance. The following steps are helpful in identifying good candidates for minimization: *a*) use materials acquisition and waste generation data to identify the chemicals used and disposed of in the highest amounts; *b*) match these against the list of PBT chemicals as well as other risk-based lists of chemicals; *c*) determine the feasibility of implementing source reduction activities; *d*) calculate the cost effectiveness; *e*) select and prioritize wastes for minimization efforts based on the assessment information gained from the previous steps.

At NIH, for example, chloroform, phenol, and lead have been identified by waste accounting systems as the three highest volume PBT chemical wastes. All three are amenable to source reduction techniques without placing burdens on research. For most radionuclides used in laboratories, other less-toxic alternatives to lead shielding are available, and use of nonradioactive methods eliminates the need for shielding entirely. Much of the chloroform and phenol is used for extraction and purification of nucleic acids. There are now substitute methods suitable for many applications that don't use these chemicals. Regarding the cost effectiveness of source reduction, phenol and chloroform are most often disposed in lab packs, which have a high cost/volume ratio. Lead is relatively inexpensive to recycle. However, when it gets contaminated with radioactive material or contaminates radioactive waste, the resulting mixed waste can be extremely expensive problems for facilities to deal with.

Many different risk-related criteria can be used for establishing priorities for minimizing wastes. The EPA PBT list is an obvious starting point. Data on other risk factors such as acute toxicity, mutagenicity, carcinogenicity, and endocrine disruption potential should be used as well. Use of such data is particularly important for chemicals that are primarily used in research rather than industrial applications, because most of these chemicals have not been evaluated for placement on priority lists. Several EPA publications (*17,67,68*) provide general guidance on prioritizing waste streams for minimization. Facilities should set waste minimization priorities based on criteria most important to their specific operational activities.

Source Reduction Strategies

Several steps should be taken in biomedical research laboratories to minimize chemical waste generation.

Use standard operating procedures. The preparation of standard operating procedures (SOPs) for common and repeated laboratory procedures offers the potential to significantly reduce chemical waste generation. Usually SOPs are driven by the desire to achieve reproducible, reliable, and accurate experimental results. When writing such procedures, consideration should also be given to the chemicals and quantities used, and the disposition of these materials with the goal of minimizing wastes. SOPs should be reviewed periodically to determine if the amount and/or toxicity of wastes could be further reduced.

Establish and maintain a chemical inventory system. Many facilities have successfully utilized computerized chemical management systems in combination with a pharmacy-type distribution facility to assist with inventory control and tracking of chemicals. Such systems significantly reduce waste generation (*69,70*). Minimally, the facility should maintain a record of users of specific chemicals. Such lists can offer the opportunity for decreasing the amounts of chemicals procured by reducing duplication of orders and sharing common chemicals among investigators.

Redistribute excess chemicals for beneficial use. All institutions should have a program to redistribute excess chemicals that are still in good condition. These programs take excess chemicals of suitable quality that laboratories inevitably accumulate and find other researchers who can make use of them. Such programs save money by avoiding both purchase and disposal costs. Essential operating features of redistribution programs include *a*) developing criteria for determining what chemicals are suitable for redistribution and quality assurance procedures; *b*) providing a safe and secure repository area for chemicals pending redistribution; *c*) establishing policies on how long chemicals remain in storage; *d*) publicizing (marketing) the availability of such chemicals; and *e*) appointing a qualified person to be in charge of the chemical repository. (Shared responsibility does not work.)

Ensure complete identification of chemicals. All chemical containers should be labeled indicating the chemical names(s) of their contents. Codes, acronyms, and other obscure identifiers should be avoided. This is particularly important for samples of chemical intermediates and final products held for future reference. These items often lose their identity once their original owner leaves the work site. Such unknown samples become very difficult to manage and cannot be transported or disposed of without accurate and complete identification.

Reduce the size of experiments. This can be accomplished by minimizing the volume of reactants, using microscale techniques, carefully selecting the appropriate experimental design (factorial, partial factorial, etc.) and the number of replicates required.

Manage chemical procurement. Avoid purchasing excess quantities of chemicals. Encourage investigators to order only what is needed for the next 3–6 months or on completion of a protocol.

Segregate hazardous wastes. This step increases recycling and management options. Keep hazardous wastes separate from biohazardous, radioactive, and nonhazardous wastes.

Maintain good housekeeping. This will help reduce spills and contamination. Areas where hazardous chemicals are stored and used should be confined to minimize size of the areas subject to contamination and spills. Avoid overuse of absorbents, liners, etc. that may require management as chemical waste.

Management of Wastes

Some generation of chemical wastes from biomedical research is unavoidable. Once source reduction strategies have been exhausted, management options must be selected to minimize the volume and toxicity of wastes and the potential environmental impacts of waste treatment and disposal. The strategies below are presented in their general order of desirability from the standpoint of environmental protection.

Recycling. Recycling processes usually require wastes to be reprocessed or reclaimed before their constituents can be used for beneficial purposes. Examples of recycling strategies for laboratories include *a*) separate collection of used solvents with only trace levels of contamination for use in washing purposes; *b*) distillation recovery of solvents for reuse (refer to examples of best practices); and *c*) segregation of wastes that have reclamation value, such as used oil, mercury, scrap lead and precious metal compounds, and solvents suitable for use in fuel recovery facilities.

Treatment. In-laboratory treatment (*71,72*) can be a valuable tool to minimize volumes of waste and reduce hazards from the handling, transportation, and disposal of hazardous wastes. Due to RCRA constraints, treatment of laboratory wastes should be limited to small amounts of chemicals used in experimental procedures and acid/base neutralizations. All treatment procedures must be carefully evaluated to ensure worker safety, effectiveness, and regulatory compliance.

Consolidation. Small containers of chemical wastes are usually packaged for shipment and disposal in lab packs (drums or other containers filled with absorbent material). Some facilities reduce the numbers of lab packs shipped off-site by consolidating the contents of small containers of compatible wastes into larger bulk containers such as 55-gal drums. This can substantially reduce shipping volumes and disposal costs. Consolidation activities usually are not considered treatment and do not require EPA permits. However, they should never be undertaken without adequate facilities and equipment, a thorough safety review, and preparations for spills.

Disposal. From the standpoint of environmental protection, disposal is the least desirable option in the heirarchy of methods used for managing chemical wastes. Disposal methods for chemicals regulated as hazardous waste are dictated by the EPA and states. For nonregulatted chemicals, the generator may determine the disposal method. In most cases, nonregulated chemicals that have unknown or potentially hazardous properties should be disposed of as hazardous waste, using incineration or other methods that assure their destruction and prevent toxic emissions. Nondestructive methods such as releasing wastes to the sanitary sewer or disposal or in landfills are only appropriate for sugars, buffers, and other low-hazard, nonregulated chemicals.

Regulatory Issues

Overview of existing regulations. Regulation of hazardous wastes under RCRA has been in place for almost 20 years. These regulations are very specific in defining what is regulated as a hazardous waste and how these wastes must be disposed. Hazardous wastes are tracked from the time they are generated through their final disposal at permitted hazardous waste disposal sites. There are limits on the amounts kept in storage and the length of time waste can be stored. Waste containers must be compatible with the wastes they contain, properly labeled, and kept closed except when in use. There are requirements for training and emergency response. Generators of hazardous waste are required to plan for minimization of wastes and must certify on each manifested shipment of hazardous wastes off-site that they have reduced the volume and toxicity of the waste to the maximum extent practical.

In addition to the regulations adopted pursuant to RCRA, regulatory schemes promulgated after several other statutes affect the management of hazardous wastes in biomedical laboratories. These include the following: Clean Water Act of 1977—CWA (*33*); Clean Air Act—CAA (*41*); Comprehensive Environmental Response, Compensation and Liability Act—CERCLA (*73*); Hazardous Materials Transportation Act—HMTA (*74*); Superfund Amendments and Reauthorization Act of 1986—SARA (*75*); and Toxic Substances and Control Act—TSCA (*76*).

Regulatory impediments to effective management. Biomedical research generates relatively small quantities of a large variety of wastes and the composition of these wastes varies dramatically over time. Because RCRA prescribes detailed characterization and tracking requirements for all regulated wastes regardless of volume, disposal of wastes from biomedical research laboratories entails a large amount of paperwork for a relatively small amount of waste. Larger biomedical research institutions may encounter regulatory difficulties in administrative areas that have little to do with sound hazardous waste management. For example, institutions that are not contiguous must obtain multiple generator identification numbers. Once this happens, transfer of wastes to a central management facility creates additional regulatory burdens due to manifesting requirements. In some cases, it may be determined that the centralization of waste management activities is not legal without a Part B permit, which is difficult and costly to obtain. Some regulators have imposed hazardous waste training requirements on researchers that appear to be excessive relative to their involvement in hazardous waste management activities. Institutions have questioned the numbers of researchers that must be trained and the extent of training required. Unnecessary, redundant or excessive training efforts consume resources that could be used more productively elsewhere in the institution.

Examples of Best Practices

Chemical redistribution program. Laboratory chemical redistribution programs (chemical exchanges) have been in place at NIH and many university and college campuses for some time. Improvements in information technology and computer networks have fostered the development of these exchange programs and greatly improved the efficiency of their operations. Automated systems now allow the posting of instantaneously updated inventories of surplus chemicals, searching for needed chemicals, and in some cases the placing of surplus pick-up and delivery orders. An example of such a system is found on the NIEHS campus. When researchers at the site have excess reagents, they send E-mail messages that broadcast to other researchers.

To increase the potential for reuse of surplus chemicals, some institutions have expanded the reach of chemical redistribution programs beyond their own facilities. An example is a program initiated several years ago by Bowling Green State University (Bowling Green, Ohio). They expanded their existing orphan chemical recycling program to include nonuniversity academic institutions such as technical colleges, high schools, junior high schools, some nonacademic facilities, and a local hazardous waste management company. The expanded program was highly successful, resulting in the transfer of 2,000 pounds of solid chemicals and 475 gallons of liquids chemicals to needy institutions and facilities. The dual cost savings associated with these transfers (for avoidance of purchase and disposal costs) were estimated to be between $150,000 and $180,000 after approximately the first year of operation (*77*).

Recovery of waste solvents by distillation. Biomedical research facilities can generate significant amounts of waste solvents. On-site recovery for reuse of high volume solvents by batch distillation can be a cost-effective technique. An example of such a recovery operation was provided by NIEHS (*64*). A review of the volumes of waste xylene and ethanol solvents generated by a centralized histology services operation led to successful development of an on-site waste solvent distillation and recovery operation as part of the overall laboratory waste minimization program at the institute. Critical to the success of the program was involving the end users in the initial steps taken to define acceptance criteria for the recycled solvent and ensure quality control.

The committee received reports of other facilities successfully recovering waste xylene and ethanol from histology operations (*78*). However, no reports of successful recovery of solvents from other laboratory uses were found. Barriers to recovery of these other solvent waste streams include the high capital cost of equipment, technical difficulties in separating pure solvents out of mixtures, regulatory concerns (some states may require permits), and acceptance of recovered solvents by the users. Therefore, distillation must be evaluated by each institution and many will find that other pollution prevention activities are more desirable.

Water conservation. An often overlooked resource in the laboratory is the water supply. Although the use of high- or ultra-purity water (e.g., deionized, distilled, 18 meg-ohm) is usually well managed through experimental protocols, the use (or misuse) of tap water is often ignored. Because high volumes of tap water are used in rinsing, cooling, and washing operations, costs associated with wastewater treatment and disposal can be significant. Investigators should consider water conservation opportunities in their ordinary tap water usage. For instance, instead of using water-cooled condensers on permanent experimental setups, a recirculating coolant system is more water resource efficient. Tap water should not be left

running in the laboratory sink. Similarly, vacuum service should be obtained from the laboratory service taps, or when not available, by vacuum pumps, instead of using water aspirators operated at the sink.

Mercury reduction programs. The committee found many examples of best practices for minimization and management of specific chemical wastes generated by biomedical research facilities. This section highlights examples of best practices to reduce the use of mercury and mercury-containing products. While mercury represents a small portion of the PBTs generated by research facilities, the potential for spills and exposures, high decontamination and disposal costs for items contaminated with mercury, and extremely low allowed discharge limits for mercury in wastewater have caused many facilities to assign high priority to mercury reduction efforts. These examples illustrate how focused pollution prevention initiatives can greatly reduce or eliminate problematic chemical waste streams in biomedical facilities.

Mercury reduction program at a research hospital. The NIH Warren G. Magnuson CC is a tertiary-care Federal hospital where NIH clinical investigators study human diseases. In 1996, CC employees addressed emerging clinical and safety concerns about the use of medical devices containing mercury. Data from the chemical spill responders and hospital hazard surveillance teams supported the safety committee's recommendation that the CC reduce its use of mercury-containing devices. At the same time, the Standardization (Equipment) Committee needed to purchase automated blood pressure monitoring equipment to meet changes in the standard of care for conscious sedation, a higher risk medical procedure recommended by both accreditation and professional organizations. After discussions with the stakeholders, the CC purchased mercury-free thermometers and sphygmomanometers for all new and existing applications. These included aneroid or mechanical blood pressure monitors and infrared and digital thermometers for routine use, and more sophisticated systems capable of measuring patient vital signs (blood pressure, temperature, and pulse rate) on a continuous basis for monitoring patients during conscious sedation. Mercury-containing devices were considered by many clinicians to be the gold standard, and their replacement with nonmercury devices was not without controversy at the CC or other institutions (*79–81*). This was anticipated by the proponents of the CC mercury reduction project, and steps were taken to involve the medical community early on and to address their concerns. On the basis of this experience, these steps should be undertaken in implementing similar reduction projects in other facilities:

a) Inform and involve all of the stakeholders including administration, clinical staff, biomedical engineering, and environmental safety personnel throughout the decision-making and implementation process.

b) Conduct a comprehensive search to identify all mercury-containing devices within the facility that may have alternatives. The CC identified safer alternatives to replace mercury esophageal dilators, canter tubes, and glass barometers and thermometers used for calibrating laboratory equipment (*82*).

c) Avoid requiring across-the-board elimination of mercury devices when alternatives may not be suitable. For example, infrared thermometers may not meet the clinicians' needs for certain patients (*83–87*).

d) Monitor trends among medical suppliers who are eliminating their use of mercury in their equipment. During the project, the CC learned that several manufacturers planned to phase out the production of mercury-containing equipment, ensuring that mercury-free replacements would be an inevitable event.

e) Divide the project into phases and set priorities for the removal of higher risk items (e.g., those frequently associated with hazardous spills). This portion of the CC mercury reduction project resulted in the removal of more than 1,500 mercury-containing medical devices and was completed without a spill incident or interruption in patient care.

Comprehensive program for tracking and elimination of mercury in facility effluent. Facing a technically difficult requirement to achieve a near-zero limit on mercury in wastewater, several hospitals and universities in the Boston area agreed to work with the Massachusetts Water Resources Authority (MWRA) and the Medical Academic and Scientific Community Organization, Inc. (MASCO), a consortium of local institutions, in developing a comprehensive control program. This included investigation of occult sources of mercury in products used by their institutions, development of source reduction measures, and evaluation of treatment technologies for removal of mercury from plumbing systems and wastewater. Source reduction methods developed by the program and actions to remove mercury-containing biomass from piping systems were the most successful approaches found and resulted in reductions of the average concentration of mercury in wastewater discharges from participating institutions by 80%. A description of the program, lists of recommendations, and resource materials are available from the MWRA/MASCO cooperative work group (*88*).

Subcommittee on Pharmaceutical Wastes

Biomedical research facilities directly dispose of small quantities of unused drugs and wastes contaminated with drugs in the course of their operations. The total amount of drugs disposed of by biomedical facilities is negligible when compared with that disposed of by society. However, drugs are primary products of research, and the impacts of their use and disposal on human health and the environment should be addressed by the biomedical research community.

The pace of biomedical research and development is increasing rapidly, and this has the potential to significantly increase the generation of waste drugs, manufacturing intermediates, and wastes contaminated by these substances. A 1999 survey reported 354 medicines currently in development for cancer alone (*89*). According to the Pharmaceutical Research Manufacturers Association, pharmaceutical companies invested $24.0 billion in research and development in 1999, a 14.1% increase over 1998 (*90*).

Sources of Waste Drugs and Related Wastes

The primary sources of drug wastes are pharmaceutical research, development, and manufacturing, and the use of drugs by patients. Only a very small percentage of the drugs disposed of by facilities and patients is unused.

Pharmaceutical research and development. The quantities and compositions of drug-related wastes generated during biomedical research activities depend on many factors, including the phase of research and the type of facility.

During the drug development phase, drug-related wastes may include compounds under investigation for potential use; chemicals used to analyze, extract, or synthesize investigational drugs; agents used in molecular studies; drugs used for testing in laboratory animals; and veterinary drugs used for care of laboratory animals.

Only about one out of every thousand compounds that undergo testing in the development phase reaches the clinical trial phase (*91*). However, wastes from the clinical trials may be more likely to be released into the environment, because wastes from this phase are usually not managed in larger, centralized facilities that tend to have well-developed waste minimization and disposal procedures.

During the clinical trial phase the drug wastes may include investigational drugs, standard-of-care drugs used to compare therapeutic efficacy of new drugs, and drugs used for the diagnosis and treatment of patients. Drug wastes may be in several forms: unused, expired, and residual drugs as solids and liquids; wastewater from cleaning areas contaminated during the mixing and administration of pharmaceuticals; and solid wastes contaminated with drugs.

Once pharmaceuticals have reached the later stages of clinical trials and after they are approved for clinical use, they are typically administered and disposed of in small healthcare facilities and households, settings where there are virtually no requirements governing disposal, and little or no guidance on appropriate disposal methods is provided to patients.

Patient excreta. Patient excreta are the primary source of drug contaminants in the environment. Data in the *Physicians' Desk Reference* (*92*) indicate that for many widely prescribed drugs, from 50 to 80% of a patient's intake of a drug is excreted as unmetabolized drug or active metabolites.

Regulation of Drug Waste Disposal

Regulations governing disposal of unused drugs vary among countries. Some countries such as Great Britain regulate disposal of all unused prescription medicines (*93*). In the United States, few regulations govern disposal of unused drugs, except for those that are specifically regulated as hazardous wastes or controlled substances. Disposal practices for drug wastes vary widely between facilities and are determined by the type of drugs present in the waste, the form of the waste, size of the facility and institutional considerations.

Drugs regulated as hazardous wastes. Of the hundreds of thousands of compounds and formulations that are in use or being investigated for potential use as drugs, only 18 are subject to regulation as hazardous waste by EPA (Table 3). The scope of regulations is very limited even for the listed drugs. The regulations generally do not apply to used drugs, drugs that are not considered commercial products, drugs in formulations that contain multiple active ingredients, unused drugs disposed of by households, and domestic sewage.

Table 3. Drugs subject to EPA hazardous waste management requirements if discarded unused.

Listed waste name	Chemical Abstracts Registry No.	EPA hazardous waste number[a]
Chlorambucil	305-03-3	U035
Cyclophosphamide	50-18-0	U058
Daunomycin	20830-81-3	U059
Diethylstilbestrol	56-53-1	U089
Epinephrine	51-43-4	P042
Formic acid	64-18-6	U123
Gallium nitrate[b]	69365-72-6	D001
Lindane	58-99-9	U129
Melphalan	148-82-3	U150
Mitomycin C	50-07-7	U010
Phenacetin	62-44-2	U187
Phenol	108-95-2	U188
Reserpine	930-55-2	U180
Resorcinol	108-46-3	U201
Streptozotocin	18883-66-4	U206
Nitroglycerine	55-63-0	P081
Uracil mustard	66-75-1	U237
Warfarin, sodium salt[c]	81-81-248	U248

[a]Listed hazardous waste (*94*). [b]Unlisted waste with regulated characteristic of ignitability when drug is in concentrated form. See Code of Federal Regulations (*95*). [c]Number applies to parent compound.

The requirements for management of drugs regulated as hazardous wastes also vary with the type and size of the facility. Waste generators are grouped into three categories based on the total amounts of hazardous wastes that they generate: large quantity generators, small generators, and conditionally exempt small-quantity generators (CESQGs) (*96,97*). Major research facilities are likely to be large generators and are subject to the most stringent regulations. Facilities that are likely to be CESQGs and subject to minimal regulation typically include small hospitals, clinics, nursing homes, assisted living facilities, and retirement communities. (It is of concern that these CESQGS often have the highest concentrations of people using multiple medications.) In most states, some generators such as households are exempt from all regulations.

Drugs and intermediates regulated as controlled substances. Controlled substances include narcotics and other drugs that may be abused. They are subject to special licensing, ordering, storage, handling, use, and disposal requirements under the Controlled Substances Act (*98*), which is enforced by the U.S. Drug Enforcement Administration (DEA) (*99–101*). Disposal procedures for controlled substances generated by pharmacies, laboratories, and medical facilities are regulated by the DEA and state agencies. These procedures are primarily intended to prevent diversion and abuse, not to protect the environment. Once a drug is prescribed, patients may dispose of any personal controlled substance in any manner they choose.

Chemical intermediates. Chemical intermediates used to synthesize drugs may be regulated as hazardous waste if they are specifically listed as hazardous wastes by EPA or have certain hazardous characteristics such as ignitability, corrosivity, or leachate toxicity.

Drugs and intermediates subject to both EPA and DEA regulations. On the DEA list of scheduled substances, only one compound, phenylacetone (Schedule II), may also be regulated by EPA as an unlisted hazardous waste. The Chemical Diversion and Trafficking Act of 1988 (*102*) resulted in regulation of additional nondrug chemicals that were being diverted from legitimate uses to illegal production of controlled substances. Control of specific chemicals was further expanded in 1993 and 1994 by the Domestic Chemical Diversion Control Act (*103*). This required tracking of transfers and registration of manufacturers, distributors, importers, or exporters of listed chemicals. Some of these are also regulated as hazardous wastes by EPA if they exhibit defined hazardous characteristics such as ignitability. Some states regulate additional controlled substances as listed hazardous wastes.

Drugs and chemicals that are regulated as both scheduled substances and hazardous wastes may be highly problematic to dispose of, as both EPA and DEA regulations must be followed. Some of the regulatory problems in managing waste controlled substances have been acknowledged by the DEA (*104*).

Solid wastes contaminated with cytotoxic drugs. Solid wastes contaminated with cytotoxic drugs are generated during formulation and administration of the drugs to patients. NIH and many other biomedical research facilities handle these contaminated solid wastes as regulated medical waste and dispose of them by incineration (*105*).

Drugs not subject to EPA or DEA regulation. The disposal of most drugs is not regulated and disposal is left to the discretion of the owner. Disposal of unregulated drugs in the sanitary sewerage system is a common practice, especially in smaller facilities and households. Pharmacy operations at research facilities may have procedures in place to return unused drugs to pharmaceutical manufacturers or arrange for secure disposal at commercial medical waste facilities. Incineration as medical waste is believed to provide adequate treatment. However, the current trend toward alternate (nonincineration) technologies for disposal of medical wastes is of concern. The efficacy of these alternate methods in assuring destruction of drugs has not been investigated.

Disposal via wastewater systems. Unused drugs and drug-contaminated liquids such as wastewater from mixing drugs and cleaning areas contaminated with drugs are usually discharged to the sanitary sewer. In most biomedical facilities, wastewater from the preparation of cytotoxic agents is an exception, because it is usually managed and disposed of as medical waste or hazardous waste.

Disposal with general solid wastes. Unused drugs and materials contaminated with drug residues may also be discarded with other solid wastes. Municipalities dispose of these wastes in sanitary landfills or by incineration.

Disposal of unused drugs by patients. Patients accumulate excess, outdated, or unused drugs at home. These are usually disposed of via the sanitary sewer or household trash. The magnitude of drugs disposed of by these methods was demonstrated by a study from the Pittsburgh Poison Center and Children's Hospital of Pittsburgh in Pittsburgh, Pennsylvania, in 1996. Of 500 people surveyed, 54% disposed of medications in the solid wastes collected by their municipality, and 35.4% flushed medications down the toilet or sink (*106*).

Contaminated excreta. Excreta from patients taking drugs are discharged to the sanitary sewer and processed at POTWs or, in areas not served by sewers, by septic systems.

Potential Environmental Impacts of Pharmaceutical Wastes

The potential environmental impacts of essentially unregulated releases of pharmaceutically active substances on ecosystems, human health, and fertility is an area of increasing concern for many biomedical scientists and EPA (*107–109*). In addition to uses of pharmaceuticals in medicine, agriculture is another major potential source of drug contamination in the environment. An example is the widespread use of antibiotics for growth promotion in livestock production (*110*).

Regardless of their source, all pharmaceuticals are eventually disposed of, and unless collected and destroyed by incineration or other effective treatment processes, they are likely to be released to the environment. Drugs have characteristics that increase their potential to be significant pollutants. Most drugs are biologically active at low dose levels. They are relatively stable under environmental conditions, and their use is increasing rapidly with a population that is growing and aging.

The fate and effects of drugs on the environment are largely unknown, because monitoring for drug contaminants in environmental media is very limited. There is no routine testing for pharmaceuticals in wastewater and drinking water, and analytic methods are either not available or deemed not cost effective (*111*). The limited data available suggest that many drugs may present potentially significant environmental impacts.

a) Many types of drugs are not degraded or removed by wastewater treatment systems or passage through soil (*107,111–116*).

b) Some drugs are already ubiquitous, mobile, and persistent in the environment. For example, clofibrate, a lipid-lowering drug, and its derivative, clofibric acid (CA), have been found in surface water, groundwater, and marine environments. In fact, the concentrations of CA found in the North Sea and samples from other environmental sources are found at the same levels as other classic environmental pollutants such as γ-hexachlorocyclohexane (*115*).

c) Drinking water treatment systems may not degrade or remove drug contaminants. Few studies of treated drinking water supplies have been completed. However, the available information suggests that treatment methods may not be effective in removing drug contaminants. For example, in a recent sampling survey, 100% of 64 samples of drinking water samples collected in Berlin, Germany, contained CA (*117*).

d) The discharge of antibiotics with wastewater may favor growth of multiple antibiotic-resistant strains of bacteria and have adverse impacts on biological wastewater treatment processes (*118–127*). Antibiotics such as the fluoroquinolones may be primary sources of genotoxicity in wastewater from hospitals (*128*).

e) Potentially carcinogenic residues of cytotoxic drugs have been found in wastewater and drinking water (*107,116,129*).

f) Drugs known to be hormonally active agents may act as endocrine disruptors and are found in environmental media and drinking water (*107,130–132*).

Additional information on the sources, fate, and potential impacts of drugs in the environment is presented in the extensive reviews by Halling-Sørensen et al. (*107*) and Daughton and Ternes (*108*).

Trends That May Affect the Generation of Drug Wastes and Their Impacts on the Environment

Increasing allocation of research to smaller facilities. This issue of drug waste management in clinical research is complicated by the trend to perform research in smaller community medical facilities. Increasingly, clinical trials are being performed in community hospitals, outpatient treatment facilities, and doctors' private offices, facilities that are subject to minimal waste disposal requirements.

Decreasing hospitalization time. There is also a trend to decrease hospitalization and increase outpatient treatment. This means some clinical trials involve treatment of patients in an outpatient setting where they will return to their homes in the community within 24 hr. Usually, no provisions have been made to instruct patients on appropriate disposal procedures for drug-related wastes generated at home, and no system is in place to monitor drug disposal in the home environment.

Increasing use of drugs for long-term therapy. An example is tamoxifen citrate, a nonsteroidal compound that can act as an antiestrogen. It is commonly used as long-term maintenance therapy for breast cancer patients and is being promoted as preventative therapy for women at high risk for developing breast cancer. A review of its pharmacological properties reveals that 65% is excreted over 2 weeks, with fecal excretion the primary route of elimination. Although less than 30% is excreted unchanged, most of the metabolites are conjugates of the drug that have activity similar to the original drug (*92*). This drug and others that are promoted for use in preventative therapy are of particular concern because they may be used by a large population of patients over long periods. The environmental load from drugs used in this manner could be substantial.

Recommendations

The subcommittee offers these recommendations to address the drug disposal issues identified in this report:

Assessment procedures for new and existing drugs should be improved. The U.S. Food and Drug Administration (FDA) is required under the National Environmental Policy Act to consider the environmental impacts of approving a drug and biologics applications as an integral part of its regulatory process (*133*). For the following reasons the process does not appear to ensure rigorous review of the potential environmental hazards posed by drugs.

a) The majority of drug products are covered by categorical exclusions and other provisions that exempt manufacturers from having to conduct an environmental assessment (*134,135*). This means that information on the environmental fate and impacts of most new pharmaceuticals will not be available.

b) Environmental impact assessments and projections of concentrations in the environment are based only on approved uses of drugs. Substantial quantities of drugs are used for nonapproved applications. Some estimates are that 50% of all drug sales and up to 80% of sales of drugs used to treat cancer patients are for off-label, or non-FDA approved, indications (*136*).

c) There are no requirements for assessment of impacts after drugs receive FDA approval.

A better system is clearly needed to ensure that the environmental hazards posed by existing and new drugs are evaluated and that a balance is achieved between the potentially competing needs of expedited drug approval and environmental impact assessment (EIA). Exemptions from the EIA process for new drugs should be based on screening criteria that consider expected stability in wastewater and drinking water treatment systems, environmental persistence, and toxicity. When information on potential use of a drug for unapproved purposes is available, this should also be considered in the EIA. Scientific data used in reviews of proposed exemptions should be obtained from all available sources, including pharmaceutical manufacturers and independent entities.

Improved analytical techniques and monitoring programs for drugs in wastewater, drinking water, and the environment are needed. The lack of monitoring data for drugs has severely limited the ability to determine *a*) the fate and impacts of drugs on the environment, *b*) the removal efficiencies of wastewater and drinking water treatment processes, *c*) the potential for human exposures, and *d*) biological effects. The high costs and lack of established analytical methods will continue to preclude widespread testing for the myriad

specific drug compounds and metabolites that may be present in environmental media. An alternative may be to use screening tools such as microbial toxicity assays to monitor drinking water and wastes before they are discharged or applied to the land. Positive assay results could be used to trigger additional testing for specific drugs or initiate more aggressive treatment measures. Development and implementation of these alternative screening tests and monitoring programs should be accelerated.

Effective technologies for removal of drugs in water and wastewater treatment processes need to be developed. The presence of drug contaminants in wastewater is inevitable. High priority should be assigned to research and development of technologies to degrade drugs in wastewater before it is released to the environment, and to remove contaminants from drinking water.

Alternative treatment technologies for medical wastes must be evaluated. New technologies such as microwave irradiation are now being used as alternatives to incineration for treatment and disposal of medical wastes. The effectiveness of these technologies in treating drug contaminants should evaluated before they are used for processing wastes that may contain these contaminants.

Reinvent the regulatory framework governing disposal. Current regulation of most aspects of drug waste disposal is minimal, fragmented, and focused on a small, arbitrarily defined list of drugs. A uniform set of regulations should be developed for disposal of all drugs. Toxicity, persistence, and environment impacts should be primary criteria for determining the drugs that are regulated, not the type and size of facility from which they are dispensed.

Improve access to disposal options. Systems for cost-effective collection and appropriate disposal of unused drugs from patients, pharmacies, healthcare providers, and facilities of all types need to be developed.

Improve awareness and training. The research community, EPA, FDA, and pharmaceutical manufacturers should work together to design educational programs to better inform investigators, healthcare providers, and patients about the potential environmental impacts of pharmaceutical use and appropriate disposal methods.

Expand the role of research facilities. Research facilities should take a leading role in developing and implementing environmentally sound procedures for collection and disposal of drug wastes.

Make provisions for better management of wastes during clinical trials. All clinical trials must be reviewed and approved by the institutional review board where the trials will be conducted. The subcommittee found no requirement for institutional review boards to consider waste minimization and disposal. Protocols should ensure that both investigators and patients receive instruction on appropriate disposal of drug-related wastes, and provisions for return of unused drugs to the research facility or other appropriate disposal outlets should be made.

Examples of Best Practices

General source reduction and minimization options. In its report on selected hospital waste streams (*68*), EPA identified options for minimization of antineoplastic drug wastes that are probably applicable to other types of drugs as well. These are presented here with some adaptations for research facilities and additional options identified by the subcommittee.

a) Purchase drugs in quantities according to need—to reduce generation of wastes.

b) Return outdated drugs to manufacturers.

c) Donate usable surplus drugs.

d) Segregate drug wastes from other wastes.

e) Further segregate drug wastes into treatability groups so as to minimize the amount of wastes that require special handling and disposal procedures e.g., cytotoxic drugs, controlled substances.

f) Dispose noncontaminated personal protective apparatus such as gowns and other items from drug administration procedures as general solid waste.

g) Use spill containment and clean-up procedures that minimize the volume of contaminated materials.

Process changes for source reduction of iv drug wastes. A project initiated by the NIH CC Pharmacy provides a specific example of how relatively simple changes in ordering, production, and distribution systems can greatly reduce generation of drug wastes. A management team reviewed dispensing procedures and found that most of the unused iv drug wastes could be eliminated by initiating a new just-in-time production and delivery system. The system automatically reorders solutions when the nursing department documents administration of a solution. This eliminates most of the wastes generated by advance ordering. Other innovative source reduction procedures identified by the team included *a*) having pharmacy staff deliver solutions to ensure proper handling during transit to patient units and correct storage on arrival at the units; *b*) purchasing premixed iv solutions with extended shelf lives whenever appropriate; *c*) mixing and activation of iv drugs and solutions at the administration site; and *d*) training of an additional pharmacy technician so that iv solutions could be mixed and dispensed around-the-clock.

After these procedures were put into place, large-volume iv drug waste was reduced from 31 to 6%, commercial premixed iv bags returned to the pharmacy dropped from 35 to 1%, and waste of customized, small-volume iv solutions was cut from 18 to about 8% (*137*).

Assured destruction of all hazardous drugs. Research facilities should employ procedures that assure appropriate management and destruction of all potentially hazardous drugs regardless of their regulatory status. Many drugs have hazardous properties similar to regulated drugs, yet there are no regulations governing their disposal. For example, of some 120 antineoplastic drugs currently in use at the NIH CC (*138*), less than 6 are regulated as hazardous waste. NIH collects all unused antineoplastic agents and manages them according to the same procedures used for regulated hazardous wastes. All antineoplastic drug wastes are incinerated as either hazardous waste or medical waste. This practice has been in place for many years (*105,139*).

Subcommittee on Radioactive Wastes

Radioactive waste is an inevitable by-product of society's current use of radionuclides in medical research, diagnosis, and treatment of disease (*140*). Waste management and disposal operations should be considered an integral part of these uses. It is wrong to regard these operations as a freestanding practice needing its own justification (*141*). Biomedical research facilities should develop a radioactive waste minimization plan to protect public health and the environment by reducing both the volume and activities of wastes they generate. Less waste also reduces potential liabilities and costs, conserves disposal capacity at the few operating waste disposal sites, and facilitates better management by the disposal site operator.

Classification and Definitions

Radioactive materials exist in nature or may be produced artificially. Regulations governing the use of radioactive materials depend on their origin. Source, special nuclear, and by-product radioactive materials are regulated by the U.S. Nuclear Regulatory Commission (NRC) or by states approved by NRC (agreement states). Any waste that contains or is contaminated with any of these materials is subject to NRC regulation. Many biomedical research institutions subject to NRC regulation will generate low-level waste (LLW). LLW is waste requiring disposal at a land disposal facility and is defined by the NRC as radioactive waste not classified as high-level radioactive waste, transuranic waste, spent nuclear fuel, or uranium or thorium mill tailings or waste. LLW is designated Class A, B, or C, depending on the

concentration of short- and long-lived radionuclides present in the waste. Most LLW generated by biomedical research facilities will fall into the category of Class A waste.

Naturally occurring or accelerator-produced radioactive materials (commonly referred to collectively as NARM) are not subject to NRC regulations or included in the definition of LLW. The generation and use of NARM is generally left to the states. Any waste containing or contaminated with NARM is not regulated by the NRC. However, these wastes still require proper disposal under state regulations.

Characterization

Most of the LLW generated by biomedical research facilities and hospitals falls into several general waste streams: dry solids, organic liquids, aqueous liquids, biological wastes, halogenated compounds, liquid scintillation wastes, and sealed sources (*142*).

Dry solid wastes consist of contaminated laboratory trash and apparatus, protective clothing, towels, paper, sharps, and packaging materials. Biomedical research facilities may also generate contaminated solid wastes from patient care.

Organic liquids include radioactive wastes that may contain alcohols, ethers, aldehydes, ketones, toluene/benzene/xylene, and other aromatic compounds. Many of these wastes are considered low-level mixed wastes, a category of multihazardous wastes.

Aqueous liquids include washings from contaminated glassware, cell culture media, buffers, and nonhazardous reagents contaminated with radioactive material.

Biological wastes include animal carcasses, human and animal tissues, bedding, excreta, and clinical samples. Radioactive biological wastes that are infectious are considered multihazardous wastes.

Halogenated wastes refers to radioactive wastes that contain regulated concentrations of one or more halogenated organic compounds such as polychlorinated biphenyls, or chloroform. These wastes are classified as mixed wastes, a category of multihazardous waste, if they are coregulated by EPA as hazardous waste.

Liquid scintillation wastes are generated when samples containing radioactive materials are analyzed using an organic substance which, when excited by the ionization of the molecules due to interaction with the radiation, emits flashes of light as the molecules fluoresce. These wastes may be considered mixed waste if they contain organic solvents such as toluene that are regulated by EPA as hazardous waste.

Sealed sources are primarily used for instrument calibration and require special precautions and preparation when offered for disposal.

Assessment of the Potential for Releases and Environmental Impacts

The total quantity and activity of radioactive waste disposed at commercial LLW sites from biomedical research is a very small fraction of the amount of commercial waste generated nationally. The National Low-Level Waste Management Program (NLLWMP) of the U.S. Department of Energy annually assesses and reports on the LLW received at commercial disposal (burial) sites. Five broad categories of generators of LLW are tracked in their reports: academic, government, industrial, medical, and utility. The volume of LLW disposed by the academic and medical categories from 1995 to 1997 ranged from 8,358 ft^3 to 11,623 ft^3, or 1.4–2.8% of the total LLW volume disposed nationally. The total radioactivity in this waste accounted for less than 0.1% of the amount disposed during these 3 years (*143–145*).

Radioactive aqueous liquid wastes containing byproduct material may be discharged to the sanitary sewer pursuant to NRC and state regulations. The total activity released each year is capped (*146*). There have been several cases of radioactive contamination discovered at sewage treatment plants, which required remediation at considerable cost (*147,148*). However, the sites requiring remediation were primarily contaminated due to radioactive discharges from industrial manufacturing operations, not biomedical research facilities.

Most of the radioactive materials used in biomedical research are short-lived radionuclides and are used in small quantities or low activity concentrations. Wastes containing only short-lived radionuclides are usually held for decay in storage on-site and then disposed of as nonradioactive waste. Even if these radionuclides were released from wastes without decay, it is unlikely that they could pose a significant threat to the environment because their half-lives are too short to allow bioaccumulation and persistence. Only two long-lived radionuclides, ^{14}C and tritium (^{3}H), find significant use in research laboratories. Neither of these isotopes is bioaccumulative.

Biomedical research facilities may also generate gaseous wastes that result from using volatile radioactive materials to label compounds. However, based on the restrictions imposed by the NRC and agreement states, the potential for significant releases and impacts on the environment from such uses is expected to be very small.

Source Reduction Strategies

There are many opportunities for biomedical research facilities to prevent the generation of radioactive wastes. Source reduction approaches employed by successful minimization programs focus on the users of radioactive materials.

a) A waste minimization training program should be established to ensure that all users of radioactive materials are aware of the importance of incorporating practices into their work that eliminate or reduce the amount of waste.

b) The use of nonradioactive alternatives for procedures that employ radioactive materials eliminates the generation of radioactive waste and should be encouraged. Nonradioactive tracers are now available for many common assays and procedures that originally used radioactive materials (*149*).

c) The amount of radioactivity used in experiments should be minimized. Investigators should purchase only those radioactive materials that will be used and avoid purchasing more when vendors offer large-quantity discounts.

d) The number of people authorized to use radioactive materials or having access to areas where these materials are used should be limited. This is also useful in maintaining exposures to radiation in accord with the as low as reasonably achievable (ALARA) standard of the NRC (*150*).

e) Segregation of waste streams in laboratories is essential. Equipment and materials should be surveyed to determine if radioactive contamination is present before they are discarded as radioactive waste.

f) The use of shorter-lived radionuclides, with half-lives less than 120 days, allows generators to hold the waste for radioactive decay. Wastes containing only short-lived radionuclides should be collected separately from wastes containing long-lived radionuclides.

g) Gaseous wastes should be controlled at the point of generation. The use of charcoal filtration to remove volatile radioactive materials, particularly radioiodines, is effective at minimizing the amount of material released to the environment via air emissions.

Management of Wastes

Recycling, reuse, volume reduction, release to sanitary sewer systems, direct releases to the environment, decay-in-storage, and land disposal are common components of radioactive waste management programs at research facilities. Options for reuse and recycling of radioactive wastes are available for a few waste streams (*151,152*). Many facilities compact wastes to reduce the volume of waste that must be shipped off-site. Industrial supercompactors may be used by waste processing companies to further reduce the volume of waste before burial. Several facilities utilize incinerators to treat radioactively contaminated biological wastes, liquid scintillation vials, and dry solid wastes (*153,154*). Vitrification of radioactive waste is now commercially available and can achieve volume reductions in the range of 200:1. Other waste

treatment methods such as alkaline hydrolysis (*155*), freeze drying (*156*), and dry distillation (*157*) may be performed on certain waste types. Aqueous liquid wastes containing byproduct materials may be discharged to the sanitary sewer, provided the facility does not exceed limits set by the NRC (*146*).

Regulatory and Political Issues

Limited availability of disposal sites. Limited access to LLW disposal facilities and rapidly rising costs of disposal are national issues that affect the biomedical research community. The U.S. General Accounting Office recently completed a report on the status of efforts by states and compacts to establish new disposal facilities (*158*). The report states

> The limited capacity of the Barnwell [SC] facility and the lack of the successful development of new facilities by compacts or states raise the question of whether to retain or abandon the compact approach. Retaining the present system would allow compacts and individual states to continue to exercise substantial control over the management and disposal of low-level radioactive wastes *but would also maintain a system that has not provided an ample, assured supply of future disposal capacity* [emphasis added].

Many research procedures cannot be performed without radioactive materials, and researchers may prefer to use them rather than alternative reagents because the techniques are well established and proven. Thus, future advances in scientific knowledge may rest on the availability of radioactive materials and the ability to safely and economically manage wastes resulting from work with them. Biomedical research must not be hindered or prevented because of the inability to provide for disposal of radioactive wastes. The research community must continue to work with local, state, and Federal agencies and encourage them to provide waste disposal capacity so these important activities may continue.

Additional restrictions may limit disposal of aqueous LLW. The NRC and EPA are conducting a joint sewage sludge radiological survey to assess the need for additional controls or regulations because of radioactive contamination at several POTWs (*159*). These may impact biomedical facilities that discharge treated aqueous LLW to the sanitary sewer.

Examples of Best Practices

Volume reduction. Dry radioactive waste volumes were reduced by over 89% using waste shredders and compactors at the Columbia-Presbyterian Medical Center (*160*).

Reduction of off-site shipments. At Harvard University, implementation of a strong decay-in-storage program resulted in a decrease from 98 to 21% in LLW shipped for disposal off-site as a percentage of the total amount of waste generated. The university also uses a waste incinerator for reducing the volume of LLW. The use of on-site incineration coupled with the decay-in-storage program has led to reductions in the amount of LLW shipped off-site for disposal to only 1.6% of the amount generated (*161*).

On-site incineration. NIEHS has also operated an incinerator for reducing the volume of waste from biological experiments (*154*). Mass reductions achieved ranged from 91 to 97%.

Other institutional programs. Descriptions of other highly successful LLW management programs include those operated by the Albany Medical Center (Albany, New York) (*155*) and the Rockefeller University (New York, New York) (*162*).

The National Low-Level Waste Management Program of the U.S. Department of Energy. The NLLWMP has published many reports dealing with all aspects of radioactive waste management summarizing successful management programs. Although is it is somewhat dated, a 1987 report provides an excellent overview of radioactive waste management practices in biomedical institutions (*163*). Current information regarding the NLLWMP may be obtained visiting the program's website (*164*).

Subcommittee on Multihazardous Wastes

This section discusses issues relating to management of multihazardous wastes. These wastes are the most problematic and costly of all of the major types of wastes generated by research facilities.

Classification

Multihazardous wastes. Wastes that contain any combination of chemical, radioactive, or biological hazard are considered multihazardous (*165*). Biomedical research facilities may generate all types of multihazardous wastes: chemical-radioactive, chemical-biohazardous, and radioactive-biohazardous. They are probably the only sources of chemical-radioactive-biohazardous wastes.

Mixed wastes. A subset of multihazardous wastes, mixed wastes, contain both LLW and chemicals regulated as hazardous wastes. Some wastes contain a mixture of hazardous waste and radioactive materials that is not regulated by the NRC and thus does not meet the regulatory definition of mixed waste, but requires special consideration due to the radiological hazards present. Mixed wastes are the most common type of multihazardous waste generated by research facilities and the primary focus of this subcommittee. The hazardous chemical portion of mixed wastes is regulated by EPA or states authorized under RCRA. The radioactive materials are subject to oversight by the NRC or the states. Additionally, mixed wastes from biomedical facilities frequently contain biohazardous agents and materials regulated as medical waste.

Characterization

Composition. Mixed waste generated in biomedical research institutions varies greatly depending on the type of research being done. The majority of mixed waste samples are generated as organic and aqueous mixtures that vary in composition from a pure radiolabeled organic compound to a crude mixture of sludge with one or more radionuclides present. Additionally, wastes such as inorganic mixtures, toxic metals, paper towels and absorbent materials, rubber gloves, debris, syringe needles, and hospital waste are also generated. The most often reported radionuclides in biomedical mixed wastes are ^{3}H, ^{14}C, ^{32}P, ^{35}S, and ^{125}I.

Sources and quantities generated. Mixed waste is produced all across the United States from processes such as medical research and pharmaceutical and biotechnology development. University and medical research institutions typically produce high volumes of aqueous waste containing low levels of radioactivity. Low to moderate waste volumes containing higher levels of ^{3}H and ^{14}C are generated from synthesis of radiolabeled compounds and other research operations.

Potential Environmental Impacts

The potential impacts of mixed wastes on the environment may be estimated based on assessments of the impacts from their chemical and radiological constituents, which are similar to those in other nonradioactive wastes and LLW from research facilities. These impacts were assessed in the previous subcommittee reports. Based on these assessments, it appears that mismanagement of mixed wastes is unlikely, and accidental releases would be likely to pose only a very low threat to human health or the environment.

Source Reduction Strategies

The implementation of waste minimization programs for mixed wastes at major research facilities has demonstrated that generation rates can be greatly decreased. The principal strategies employed for source reduction of mixed wastes are similar to those for biohazardous, chemical, and radioactive wastes (*162,166,167*). Particular emphasis is placed on strict adherence to segregation requirements. By keeping radioactive and chemical wastes separate, generation of many types of mixed wastes can be eliminated and management efforts can be focused on unavoidable mixed wastes. The

use of commercial laboratories to prepare labeled compounds and reagents is also an important strategy to reduce or eliminate generation of high-activity mixed wastes that are extremely expensive to treat and dispose of.

Management of Wastes

Once generated, mixed wastes must be fully characterized and separated into common classes based on available treatment and disposal options. Most wastes can be expeditiously disposed in an environmentally benign manner. Disposal options for a few types of mixed waste are limited or nonexistent and therefore, once generated, the wastes may require indefinite on-site storage.

Recovery and recycling. Liquid scintillation counting fluids and vials and some contaminated nonhalogenated solvents are routinely shipped to commercial facilities for use as fuel supplements. At this time, recovery of the radioactive materials or chemical components from most liquid mixed wastes is laborious and not practical. Only a small portion of the solid mixed waste generated, such as contaminated mercury and lead, is recovered and reused. For mixed wastes with multicurie quantities of ^{3}H, technology is available that would allow for the recovery and recycling of ^{3}H. This would eliminate the release of radioactivity into the environment. Currently, however, recycling opportunities are not available because of regulatory issues and the lack of commercial recovery facilities.

Treatment and disposal. The treatment objective for multihazardous wastes is reduction to a waste that presents a single hazard, which can then be managed as a chemical, radioactive, or medical waste. The sequence of treatment methods should be according to the degree of risk posed by the various hazardous constituents (*165*). Examples of currently available disposal options for treatment and disposal include *a*) storage of wastes containing short half-life radionuclides for decay. The waste is held until the radioactivity has decayed, and the remaining hazardous chemical waste is disposed using an approved RCRA facility; *b*) on-site treatment of hazardous chemical constiuents where regulations and permitting requirements have been met; *c*) treatment or recycling and disposal at a commercial EPA-permitted/NRC-licensed facility using a thermal process (energy recovery or incineration); *d*) land burial of treated waste residues in approved facilities; and *e*) disposal to a sanitary sewer system, e.g., wastes generated from human clinical and diagnostic studies.

Long-term on-site storage. For wastes containing long half-lived radionuclides and those for which there are limited or no disposal options, indefinite on-site storage may be required.

Regulatory Issues

Management of multihazardous wastes is complicated by an array of Federal, state, and local requirements that may be inconsistent with the relative risk of each hazardous constituent in the waste. The current regulatory framework for mixed wastes is illustrative.

Overview of existing mixed waste regulations. Once generated, mixed waste must be transported, stored, treated, and disposed in compliance with the multiple statutes and regulations of the DOT, EPA, NRC, and state and local governments. EPA requires that a RCRA permit be obtained to treat or store waste on site. However, most research organizations elect not to obtain one because of the high regulatory burden associated with acquiring and complying with the permit. Consequently, many institutions have only limited treatment and storage options available for managing and disposing of these wastes. To alleviate some of the problem, EPA has established a relaxed enforcement policy that allows generators to indefinitely store wastes for which no treatment or disposal capacity currently exists (*168*).

The NRC's role in regulating mixed waste is to assure that safe radiation practices are maintained. For land burial of radioactive waste containing biohazardous materials, the NRC requires that the material first be sterilized to reduce the potential hazards of these materials (*169*). The commission's regulations also require that a licensed facility monitor effluent releases and maintain them to be ALARA.

States have an important authority for protecting the public from the potential hazards associated with mixed waste, and many are authorized or "agreement states" responsible for inspection, enforcement, and licensing responsibilities for users of hazardous chemicals and radioactive materials. Some states are authorized to issue permits for waste treatment; however, they may impose additional requirements or constraints.

Regulatory impediments to effective management. EPA policies and regulations intended for industrial-scale volumes of hazardous waste place enormous economic and regulatory burdens on small-volume mixed waste generators. Additionally, oversight by multiple regulating agencies further increases the management problem. Currently, the regulations do not appropriately consider the burden relative to *a*) the variety and small volumes of mixed wastes; *b*) the prohibitively high costs associated with management and disposal; *c*) the redundancies and inconsistencies that result from oversight by multiple regulatory agencies; and *d*) the lack of flexibility to allow best practices to be used for treatment and disposal of these wastes.

Therefore, research institutions are required to expend an enormous and costly effort to segregate and track thousands of small volume waste streams to comply with the regulations (*170,171*). Additionally, because of these impacts, many laboratories have placed restrictions on the generation of mixed waste and require investigators to develop alternative research methods and procedures that may not be as effective as isotopic methods.

Many of the problems confronting research facilities in management of mixed waste result from the current dual (EPA/NRC) regulatory framework. EPA recently developed a comprehensive proposal to reduce burdens associated with this framework (*172*).

Examples of Best Practices

The NIH Mixed Waste Minimization Program. Proper management and waste minimization efforts have demonstrated that a large portion of mixed waste currently being generated can be reduced or eliminated (*170*). At NIH, generation rates were decreased significantly, even though the number of research studies was rapidly increasing.

Ultraviolet peroxidation treatment of aqueous mixed wastes. A modified version of a commercially available ultraviolet peroxidation (UVP) treatment system has been developed and used to degrade hazardous organic compounds in high-volume aqueous mixed waste streams from biomedical research (*170*). UVP uses hydrogen peroxide and ultraviolet light to oxidize organic compounds to carbon dioxide and water. The system has a demonstrated removal efficiency for a number of volatile and semivolatile compounds in excess of 99.99%. No hazardous air emissions or residues are produced by the treatment process. Treated wastewater from the UVP system can be discharged to the sanitary sewer.

Catalytic oxidation treatment process for wastes containing higher activity. A catalytic chemical oxidation process has been extensively studied for the on-site treatment of mixed wastes containing hazardous chemicals and high levels of ^{3}H and ^{14}C radionuclides (*173*). Both organic and aqueous mixtures can be accommodated without sample pretreatment, and destruction and removal efficiencies of 99.999–99.99999% are achieved for most organic substances. The radioactive waste products from the process, either tritiated water or ^{14}C carbon dioxide are recovered using a simple trapping system without release to the environment.

Subcommittee on Solid Wastes and Recycling

Characterization of Wastes from Research Facilities

Biomedical research facilities generate significant quantities of general solid wastes. Wastes in this category are considered nonhazardous;

they generally will not cause or significantly contribute to an increase in serious irreversible or incapacitating reversible illness or pose a substantial present or potential hazard to human health, safety, or welfare. When properly managed, they should pose no significant adverse effects on the environment. The characterization of general solid wastes generated from biomedical research facilities is often similar to municipal solid waste (MSW) (*174,175*). Additionally, biomedical facilities may generate some forms of solid wastes that are not considered MSW, such as ash from medical waste incineration and animal bedding.

Conventional solid wastes from biomedical research facilities are generally managed in the same way as similar wastes from other sources. However, some aspects of research facility operations affect the characterization of the wastes that are generated and their management requirements. It is often necessary to modify the solid waste source reduction, recycling, collection, and disposal strategies that are in general use for applications at research facilities. First, it is of paramount importance that all necessary precautions are taken to ensure strict segregation of hazardous wastes and items perceived as hazardous from wastes that will be disposed of as general waste. In most laboratories and other research facilities, hazardous materials are used and disposed of in close proximity to nonhazardous materials. This raises the potential for inadvertent mingling of hazardous and nonhazardous wastes that can have very serious consequences.

Second, characteristics of the general solid waste streams from many facilities complicate development of recycling programs and limit the types of wastes that can be reused or recycled in an efficient and cost-effective manner.

Reuse and Recycling Options

The preferred disposition of unwanted items is transferring them to others for reuse or other uses that do not require reprocessing. Reuse, as compared to reclamation of materials from waste (recycling), conserves the most value, usually requires the least amount of energy, and generates less pollution and secondary waste.

Many research facilities have developed successful solid waste recycling programs, particularly for commodities such as aluminum, cardboard, paper, and glass that are commonly recovered from MSW. Although the prices paid for such materials are usually not a major source of income to facilities, diversion of these materials from the solid waste stream eliminates disposal charges, which may be significant. Recycling of materials from BRW is more problematic and not widely practiced:

a) Laboratories and other biomedical research areas typically generate quantities of recyclable materials that may not sufficient to justify the management burdens, space, and costs associated with development and operation of segregated collection, storage, and shipping systems.

b) Recycling facilities may not accept small lots of recyclable materials because of high overhead costs associated with handling, quality control, reprocessing, and accounting. For example, waste streams from laboratories and photoprocessing operations may contain recoverable precious metals such as silver, gold, platinum, and osmium. Even though these are very valuable materials, the costs of transporting wastes to reclamation facilities, assays, record keeping, and processing small quantities of these wastes often far exceed their recovery value.

c) Some potentially recyclable materials are unique to research facilities or have characteristics that severely limit their market value. For example, flint glass typically used in beverage containers is relatively easy to sort, melt, and reprocess into usable products. There are commercial markets for it and it is widely recycled. However, laboratory glassware and some reagent bottles are made of borosilicate glass that has a very high melting point and may not meet the acceptance specifications of recycling facilities.

d) Plastics are another example of materials that are commonly recovered from MSW but usually not good candidates for recycling from laboratory waste streams. Plastic items have recovery value if they are sorted by resin content and made from resins that are widely used in commercial products. The plastics found in MSW consist of relatively few resins, and the resin content of most common items such as beverage containers is readily identified by numbered symbols embossed on the container. This facilitates sorting and recovery. In contrast, plastics used in items for laboratory and medical applications are made from a wider variety of resins, and these are often not identified on the items. Some resins that find use in laboratory ware such as tetrafluoroethylene have few if any recycling outlets.

Waste streams that are the best candidates for recycling have established commercial markets, are generated in high volumes, and consist of relatively pure materials free of contaminants that interfere with the recycling process. For optimal recovery value, recyclable wastes must be segregated from other materials, collected, and shipped in accordance with the specifications of the receiving facility. Receiving facilities usually have a low tolerance for contaminants. Small amounts of contaminants may result in the rejection of large lots of recyclable materials or severe downgrading prices paid for these materials.

Examples of Best Practices

MERCI—An exemplary institutional program for solid waste reduction and recovery of valuable materials. A program conceived at the University of Virginia in Charlottesville, Virginia, titled Medical Equipment Recovery of Clean Inventory (MERCI) was developed to ensure efficient waste stream management and to affect a global reduction in solid waste generation and disposal costs (*176*). A major emphasis of the program was to systematically divert clean, usable materials, or "gold wastes," from incineration to charitable organizations or back into the university's medical center and research laboratories. Examples of supplies diverted from operating room wastes for reuse in biomedical research laboratories include the following:

a) Gowns that could be used as clean protective clothing for workers in research laboratories. These were found to be of better quality than cover gowns available for purchase, and they were provided at no cost to the laboratories by the MERCI program.

b) Surgical drapes for use as lab bench top covers.

c) Paper operating room towels used for linings on trays, counters, and other surfaces.

d) Numerous examples of specialized items salvaged from operating rooms that research laboratories use in their work, e.g., needle counters.

Eight years following its inception, the program has evolved into a total integrated waste management system, capturing over 73 tons of medical supplies for use in research laboratories or donation to charitable organizations. Ultimately, these data suggest a savings of 15.5 million dollars in supplies that would have been incinerated. Waste stream audit information stemming from this program was also used to streamline the use of medical supplies at the university.

Recycling program at NIEHS. The solid waste management program operated on the campus of NIEHS provides an example of a comprehensive solid waste recycling program at a major biomedical research facility. Large quantities of materials destined for a landfill or incineration are now being diverted by source reduction and recycling initiatives. Source reduction activities at NIEHS include the following:

Redistribution or donation of surplus materials. Surplus materials are first made available to all employees at a waste-exchange area located on the campus. Materials and supplies that are not claimed there are often donated to local community colleges and schools.

Paperless reports. Research studies result in the production of many voluminous reports. Instead of distributing paper copies to interested parties, the facility now sends electronic

copies, saving significant amounts of paper and postage. Many studies required 12 or more copies of reports, typically 200–300 pages long. These are now distributed electronically without paper.

Computer recycling. Computers and old equipment outdated for NIEHS use yet serviceable are made available to local schools, colleges, and universities.

Major recyclable general solid wastes streams at NIEHS include white paper, fiber paper, glossy paper, newspaper, aluminum beverage cans, steel "tin" cans, consumer plastics (beverage bottles), and glass. Table 4 lists the types of materials and amounts recycled on the NIEHS campus since February 1993. The total amount of material recycled is approaching 1,000 metric tons. The facility currently recovers about 25% of its solid waste stream for recycling.

Subcommittee on Training

Training is one of the most critical components of effective waste management programs and is mandatory for all personnel involved in generation, handling, and management of wastes in biomedical research facilities. A clear understanding of all regulatory requirements, job responsibilities, and institutional procedures for waste minimization and management is crucial for ensuring the facility's regulatory compliance and protection of health and safety, research resources, and the environment. Adoption of good laboratory waste practices also carries with it a tremendous potential for designing pollution out of future industrial processes (*177*). This is a concept that can also be applied to biomedical research facilities and the products of their research that may ultimately be used on a large scale in medicine. Well-designed waste management training programs not only teach institutional waste management practices but also improve awareness of general pollution prevention concepts. Such training programs can help create a new generation of investigators, facility operators, healthcare workers, and patients that is more environmentally conscious and informed.

Overview of Regulatory Requirements for Training

Federal, state, and local governmental agencies, as well as numerous accreditation organizations, regulate biomedical research and healthcare institutions and stipulate training requirements. This section provides an overview of training required by Federal agencies.

U.S. Environmental Protection Agency. Training requirements for hazardous waste generators are specified in EPA regulations (*178,179*). The training program must include instruction on all aspects of hazardous waste management relevant to the position in which personnel are employed, including contingency plan implementation. Topics that should be in the curriculum include *a*) requirements of RCRA and applicable state and local regulations, *b*) waste minimization techniques, *c*) hazardous waste identification and classification, *d*) hazardous waste accumulation and storage procedures, *e*) record keeping and reporting requirements, *f*) emergency response procedures and systems, *g*) potential liabilities associated with mismanagement of wastes, and *h*) employees who respond to hazardous substance releases other than those classified as incidental spills must also be trained in accordance with the hazardous waste operations (HAZWOPER) standard (*180*).

For all employees, training records must be kept on file and include specific documentation (*179*).

U.S. Nuclear Regulatory Commission. The NRC promulgates training regulations for individuals who work in or frequent areas where radioactive materials or wastes are used or stored (*181*). Laboratory workers who work in these restricted areas must receive information and training on the applicable provisions of NRC regulations and licenses for the protection of personnel from exposure to radioactive materials, including *a*) information on the storage, transfer, and use of radiation, radioactive materials, and waste; *b*) health protection problems associated with exposure to radiation and/or radioactive materials; *c*) precautions or procedures to follow to minimize exposure; *d*) purpose and function of protective devices; *e*) responsibilities and procedures for promptly reporting any condition that may cause a violation of NRC regulations and licenses or unnecessary exposure to radioactive material; *f*) procedures for responding to warnings made in the event of any unusual occurrence or malfunction that may involve exposure to radiation and/or radioactive materials such as spills of radioactive materials; and *g*) radiation exposure reports, which workers may request (*182*).

Occupational Safety and Health Administration. The Occupational Safety and Health Administration (OSHA) promulgates health and safety general and specific standards, many of which include training requirements applicable to waste management activities in research facilities. Laboratory workers exposed to hazardous materials and wastes in the workplace must be trained in accordance with the OSHA Hazard Communication (HAZCOM) Standard (*183*). The Bloodborne Pathogens Standard (*184*) deals with regulated medical waste and prevention of occupational exposures to biohazardous agents and stipulates specific training requirements. Other OSHA requirements of general application such as standards for the use of personal protective equipment (PPE) include training requirements that may affect personnel required to use PPE in waste management operations.

In some circumstances, laboratory workers may be required to participate in emergency responses to hazardous materials incidents or participate in operations at waste storage, treatment, and disposal facilities. Under OSHA regulations, such personnel are designated HAZWOPER employees and must complete a program of specific health and safety training and periodic refresher courses. NIEHS sponsored a workshop that established minimum criteria for determining the quality of worker health and safety training programs necessary to meet the training requirements specified in these HAZWOPER training standards. The results of this workshop were adopted by OSHA as Appendix E of the regulation (*185*).

U.S. Department of Transportation. The DOT regulates the packaging, labeling, transportation, and shipping of wastes that are defined as hazardous materials (HAZMAT). All employees who package, ship, receive, unload, inspect, or certify HAZMAT shipments are designated HAZMAT employees and must receive DOT training. The training must include general awareness and familiarization with hazardous materials, safety precautions, and function-specific training that addresses DOT regulatory requirements as applied to an employee's job responsibilities.

A record of current training inclusive of the preceding 3 years must be kept on file for

Table 4. Materials recycled at the NIEHS since February 1993.

Recovered material	Amount (kg)	% of total
White paper	307,386	32.5
Corrugated cardboard	175,190	18.5
Fiber paper	161,725	17.1
Magazines	137,871	14.6
Newspaper	60,468	6.4
Wood pallets	37,514	4.0
Tyvec garments[a]	23,881	2.5
Aluminum beverage cans	8,250	0.9
Wastes suitable for vermicomposting[a]	8,812	0.9
Phone books	8,135	0.9
Consumer plastic and glass containers	6,254	0.7
Molded polystyrene foam and "peanuts"[a]	2,302	0.2
Polypropylene pipette tip boxes	2159	0.2
Steel cans	1,282	0.1
Other (books, film, plastic lab ware, shredded paper, 3-ring binders,[a] plastic drums,[a] animal boxes,[a] reagent bottles,[a] ice bags[a])	3,872	0.4
Totals	944,471	100.0

[a]Items recovered by employees independent of the NIEHS recycling contract.

each HAZMAT employee. Training records must include specific documentation (*186*).

Elements of Successful Training Programs

Waste minimization training programs focused on laboratory and healthcare personnel have been one of the most effective strategies for affecting significant reductions in waste generation at biomedical facilities. Effective training programs not only provide instruction on proper waste management practices but also encourage employee cooperation by improving awareness of the costs and impacts of waste disposal, and how the actions of each employee contribute to meeting the waste reduction goals of the entire institution.

Delivery of training. Classes and training materials must be designed to meet the special needs of biomedical facility operations. They should be *a*) tailored to meet specific needs and educational levels, which vary widely among investigators, students, facility support personnel, and patients who make up the audience; *b*) flexible to accommodate rapid change; *c*) easy to use, schedule, and update; and *d*) multilingual and multicultural as determined by the composition of the audience.

Frequency of training. Training should be provided to all new employees and on a periodic basis as refresher or update service for existing employees. Additional training may be necessary, e.g., when a researcher moves to a new laboratory with different technical responsibilities or whenever substantial changes in procedures occur that affect waste generation or management. The initial training for new employees should be formal and can be combined with training required for radiation safety, general safety, or other research programs. Follow-up training can be completed during staff meetings or regularly scheduled safety meetings. Such training sessions also can be a good time to solicit waste minimization ideas from staff or to identify team members who can assist in implementing specific waste minimization opportunities.

Use of advanced training technologies. The development and application of advanced training technologies (ATT) has expanded over recent years and is expected to expand further. Computer-based training, Internet or web-based training, distance learning, teleconferencing, multimedia, and courseware applications for use in training programs are not only emerging, but many are well established. Environmental health and safety departments at many academic and research institutions use web sites for providing waste management guidance and training to students, faculty members, and researchers. In some cases, training can be completed entirely online. NIEHS conducted a technical workshop on ATT 20–21 April 1999 (*187*). This workshop focused on the application of computer and web-based training methods for safety and health training programs. The final report gives excellent background information on ATT methodologies.

Continuous program evaluation and improvement. All training program plans should incorporate provisions for performance measurement, feedback, and continuous improvement. Successful programs must be able to demonstrate that what was taught is being practiced at the work site. This is an important part of the facility evaluation processes used by surveyors such as those from the Joint Committee on Accreditation of Healthcare Organizations (JCAHO) (*188,189*).

Recommendations

Eliminate redundant training requirements. Some of the training and documentation requirements of the various regulatory agencies are redundant and should be consolidated or eliminated.

Train students at all educational levels. Curricula for students in college level biomedical disciplines should include instruction on pollution prevention and waste management. Additionally, programs should be developed to reach students in the early years of their education from kindergarten through high school.

Provide outpatient training. Programs must be developed for addressing training needs of audiences outside of the regulated community, such as patients living at home. Home-generated wastes must be properly managed to minimize risks to the environment, solid waste workers, and the patients themselves.

Examples of Best Practices

The subcommittee found that many biomedical institutions and organizations have developed innovative and highly effective programs, standards, courses, guidance documents, and other materials for waste management training. Some of these best practices are described below.

NIH Waste Disposal Guide. All research laboratories at NIH receive summary information on segregation, packaging, and disposal of various types of wastes in a pamphlet that summarizes proper segregation, labeling, and disposal practices (*190*). The pamphlet is published in a calendar format that can be mounted on the wall. Lift-up pages for each "month" provide a ready-reference source of information on segregation and management methods for various types of waste. Telephone numbers to obtain technical assistance, collection containers, waste removal, and other services are also provided. This guide is also available on the Internet (*191*).

NIH mixed waste training videos. NIH produced two videos to augment its mixed waste training program. The first video is titled "Mixed Waste: A Major Issue in Biomedical Research" (*192*). It provides an overview of mixed waste management issues and includes presentations by several NIH investigators describing innovative strategies they have developed to minimize mixed waste in their laboratories. A second film was produced in 1995 to review concepts presented in the first film and to provide an update on new mixed waste management issues (*193*).

The Medical Waste Institute—Transportation of Regulated Medical Waste Compliance Assistance Document. The Medical Waste Institute has prepared a compliance guidance document for the transportation of regulated medical waste (*194*). This document is concise, easy to read, and provides an excellent summary of the DOT requirements for packaging, identification, and transportation of RMW.

Association of Operating Room Nurses guidance document. The Association of Operating Room Nurses (AORN) issued its "Recommended Practices for Environmental Responsibility in the Practice Setting" in October 1993. This guidance document recommends practices for waste management to reduce the risk of infection, ensure regulatory compliance and resource conservation, and promote cost containment (*195*). Many organizations have adopted the waste handling guidelines of AORN. The guidance document is also useful as a reference for preparation of training courses.

Joint Commission on Accreditation of Healthcare Organizations standard. The JCAHO has included proper waste management procedures as part of their accreditation criteria. Their "Standards for Hazardous Materials and Waste" affirms the importance of training: "As with the entire JCACO program, proper procedures and employee training are key factors, as is evaluating actions for their effectiveness" (*196*).

Summary Findings

This section summarizes the findings of the subcommittees as they relate to the general issues addressed by the conference.

Potential Impacts of Biomedical Research Wastes on the Environment

All information available to the committee suggests that the potential for significant impacts on the general environment from wastes generated by biomedical research facilities is low.

a) For all waste streams studied, the contribution of research facilities to the total amounts of wastes generated in the United States is very small relative to other sectors in the economy.

b) Hazardous substances used by research facilities are stored and handled in small containers and apparatus, and points of use for these substances are usually scattered among the numerous separate laboratories and buildings. The probability of a catastrophic event resulting in the uncontrolled release of large quantities of hazardous substances is low.

c) Larger quantities of hazardous substances may be processed and stored at centralized waste collection, processing, and storage areas located on these facilities. However, requirements for containment, monitoring, and control of wastes are significantly more stringent than those imposed on substances with similar or greater hazards that are not waste. Hazardous wastes are also subject to storage time and inventory limits that do not apply to hazardous substances that are not wastes.

d) Because the quantities of hazardous substances in use and disposed of by research facilities are usually small, uncontrolled releases would be likely to impact only localized areas, not the general environment. The specific characteristics and management requirements for the various types of hazardous constituents commonly present in BRW tend to reduce the potential for releases and adverse impacts even if they are released.

e) Regulations require use of final waste treatment and disposal technologies that are protective of the environment.

f) Increasing implementation of pollution prevention and waste minimization programs by research facilities is reducing the amounts of waste generated by research procedures and the environmental toxicity of unavoidable wastes.

An exception to this assessment of a low potential for impacts are wastes containing antibiotics, antineoplastic agents, hormones, and other unregulated drugs that are released and may be persistent and toxic in the environment. Although the amounts of these substances disposed of by research facilities are miniscule in comparison with the total amounts used and disposed of by society, they are arguably the products of biomedical research and thus should be of concern.

Regulatory Issues Affecting Waste Minimization and Management

Impacts on research facilities. Virtually all aspects of waste management are governed by a complex array of Federal, state and local laws, regulations, and permit requirements. Additionally, research facilities may also be subject to requirements imposed by nongovernmental agencies such as the American Association for Accreditation of Laboratory Animal Care and multiple agencies concerned with safety and the quality of medical care (*197*). The poor fit of many waste management regulations to the operations of laboratories is well known. Much of this problem stems from the fact that the current regulatory framework was promulgated to control wastes from manufacturing and other large-scale sources of waste. Laboratories and research facilities have many unique characteristics that differ significantly from these sources (Table 5). These differences greatly influence the characterization of wastes and how they can be most efficiently controlled and regulated. Regulatory agencies have only recently begun to understand the importance of these differences in dealing with compliance issues (*199*).

Burdens attributed to the misfit regulations on research facilities were identified as major issues by this committee and have been reported by others for some time. (For this discussion, regulatory requirements are referred to as burdensome if they could be made more efficient without diminishing the intended level of protection for the environment.)

The most burdensome regulations on research facilities are those associated with hazardous waste. A planning group of the National Research Council recognized that there were problems with hazardous waste regulations as early as 1981, shortly after adoption of the Federal regulations by EPA (*200*). Similar burdens from state hazardous waste regulations have also been reported (*201*).

Recommendations for regulatory reform have been repeatedly made by the National Research Council, the American Chemical Society, and others for years. Until recently there was little action on these recommendations, as regulatory agencies gave priority in their regulatory agendas to improving control of large sources of waste and pollution. Now several initiatives are underway that may lead to significant reductions in unnecessary regulatory burdens on research operations. Examples include the following:

a) The New England Laboratory XL Project, a collaborative 4-year pilot project between three academic institutions and EPA Region I to devise a flexible, performance-based system for managing laboratory waste (*202*).

b) A collaborative project by the Howard Hughes Medical Institute in Chevy Chase, Maryland, titled "Managing Hazardous Wastes in Academic Research Institutions" (*203*). The project has 10 participating academic research institutions working with officials from EPA, state regulatory agencies, and the scientific community to develop and demonstrate best practices for managing hazardous wastes and a regulatory model for implementation by Federal and state agencies.

Table 5. Comparison of biomedical research and manufacturing facility operations.[a]

Characteristic	Manufacturing	Research
Number of chemicals in use	Low	High
Quantities of hazardous chemicals	High	Low
Likelihood of creating new substances	Low	High
Use of biohazardous agents	None	High
Use of radioactive materials	Low	High
Activity of radioactive materials used	High	Low
Variability in operations	Low	High
Staff education level	Low	High
Centralized management	High	Low

[a]Data adapted from Priznar (*198*).

An initiative undertaken by NIH to improve the effectiveness and efficiency of its overall research mission by reducing regulatory burdens experienced by the research community. The initiative was requested by the House Committee on Appropriations in its report on the FY 1998 budget. Hazardous waste management regulations were one of the five areas of investigation that comprised the initial focus of the effort (*204*).

Regulations proposed by EPA to reduce burdens associated with dual regulation of mixed wastes (*172*).

The Department of Toxic Substances Control of the California Environmental Protection Agency convened a task force to make recommendations for reform of hazardous waste regulations affecting laboratories. A bill adopting recommendations of the task force was passed by the California Assembly (*205*).

Impacts on applications of research. An issue that has received little attention is the potential impact of burdensome waste regulations on the applications of research in medicine. New diagnostic and therapeutic procedures developed through the research enterprise will undoubtedly result in the generation of new types of wastes that are problematic to manage under the present regulatory framework. As these procedures are approved and applied in medicine, the tasks of managing the resulting wastes will have to be assumed by hospitals and other healthcare facilities. These facilities may be reluctant or unable to perform procedures that generate wastes that are very costly or difficult to manage, or may expose them to serious regulatory compliance problems.

Here is an example of such a situation. Newly developed perfusion chemotherapy procedures have been developed that have the potential to significantly improve treatment outcomes in melanomas and other forms of cancer that previously had very low survival

rates with all other available treatment regimes (*206–210*). The procedures allow isolation and regional treatment of the liver, other organs, and limbs, using anticancer agents in concentrations that cannot be tolerated systemically. Radioactive tracers (usually ^{131}I) are used to monitor the procedure and ensure that blood from the region being treated does not enter the general circulation. Body fluids and solid wastes contaminated with cytotoxic drugs and radioactive materials are generated by the procedure. These multihazardous wastes may be subject to concurrent regulation as medical waste, hazardous waste, and radioactive waste. The usual processing scheme for these wastes is to store them in a frozen state for several months until the radioactive material has decayed and then manage them as nonradioactive wastes. Most hospitals probably are not equipped to manage and store this type of waste. In any case, if the waste were regulated as hazardous in their state, they would probably be prohibited from storing it because storage over 90 days generally requires a RCRA storage permit. NRC regulations would prohibit release of the undecayed waste to hazardous waste or medical waste facilities not licensed to accept radioactive materials. Even after decay, disposal of the resulting nonradioactive waste could be problematic. Most chemical waste facilities will not accept regulated medical waste, and medical waste facilities are not permitted to accept hazardous wastes. In short, there may be no legal options for storing or disposing of the waste from perfusion procedures.

Status of Waste Minimization Programs in Research Facilities

Program expansion. Highly successful waste minimization programs are being implemented at a number of major research facilities. Over 90% of laboratories in a recent survey were engaged in waste minimization (*211*). This trend mirrors the increasing emphasis on pollution prevention and the shift from waste management to materials management that is occurring in hospitals and healthcare facilities (*212*). Programs at research facilities most commonly include initiatives to encourage increased recycling of general solid wastes and source reduction efforts aimed at reducing generation of hazardous and radioactive wastes that have high management costs or limited disposal options.

Key elements of successful programs. The most successful minimization programs include three key elements: support of top management, emphasis on training of investigators on source reduction techniques, and a system to prioritize waste streams for focused minimization effort.

Compatibility of minimization programs with research. No conflicts between minimization initiatives and the needs of research were reported to the committee. Investigators are generally supportive and cooperative once *a*) they understand the intent of these initiatives and how their actions relate to program goals, and *b*) access to information on specific methods for reducing waste is provided.

In planning minimization programs, their impacts on the research mission must be carefully considered. Minimization guidance provided to investigators should be voluntary. Setting arbitrary quantitative goals for reduction of waste, a common practice in industry, should be avoided. Alternative materials and research methods recommended to meet minimization objectives must compare favorably with established methods. In some cases, it may be not be feasible to change materials and methods that are the basis of validated research. Changes may also require lengthy regulatory approval processes or new equipment, which may not be available.

In some situations, strategies primarily intended to reduce use of hazardous materials and waste generation may have side benefits in increased scientific productivity. An example of this is the use of chemiluminescent reagents and other alternatives to radioactive materials. These alternatives offer several major benefits from the standpoint of scientific productivity, including greater stability of reagents, cost savings in procurement and storage of components, and reduced security and training requirements. Over the long term, development of novel nonradioactive approaches may lead to wholly new scientific and medical technologies that may have broad societal impact (*206*).

Results of minimization programs. Implementation of minimization programs at research facilities has resulted in significant reductions in waste generation, even at facilities such as NIH that have rapidly expanding research programs. Substantial cost savings have also been reported. Although only a small number of respondents to the survey by Leonard and Reinhardt (*204*) had data on net savings from laboratory waste minimization efforts, the range reported per laboratory facility was from $10,000 to $135,000 annually. Reductions in mixed waste generation achieved by the minimization program established by NIH have avoided disposal costs of several million dollars in the last 5 years.

These findings, while encouraging, also underscore the need for institutions to improve documentation of laboratory waste minimization programs and their associated cost savings. Not only will this pass on valuable information to other institutions, but it also allows for better planning and setting of priorities for waste minimization programs.

Trends and the Future of Waste Management

Influence of research trends. Biomedical research is a highly dynamic endeavor in both its direction and methods. Changes in the focus of investigation and the technologies used to conduct research occur rapidly. In recent years, most of these changes have resulted in significant reductions in the volumes, composition, and environmental hazards posed by research wastes. Some recent examples:

Less use of highly reactive chemicals. The general trend in research emphasis away from medicinal chemistry and toward molecular biology has significantly decreased use and disposal of highly reactive chemical compounds used in synthesis of investigational drugs.

Improved liquid scintillation counting methods. For many years, liquid scintillation counting (LSC) was one of the most widely used analytic methods in biomedical research, and LSC wastes have been a major and problematic component of radioactive waste streams. LSC produces numerous small vials containing spent counting fluids that used to be predominantly composed of a hazardous organic solvent such as xylene, toluene, or pseudocumene contaminated with radioactive materials. Counting fluids were subsequently developed that do not contain hazardous solvents (*214*), and these can now be used for most counting applications. There have also been changes in counting technology that allow counting to be performed with reduced generation of wastes. These include the use of smaller-volume LSC vials (*215*) and dry counting methods (*216*) that can eliminate LSC wastes. The impact of these changes in LSC technology has been dramatic. In 1979, NIH generated approximately 2,000 55-gal drums of LSC vials for shipment to off-site recycling and disposal facilities (*170*). Generation has declined continuously since then (*171*). In 1998, only 265 drums were generated, and of these, less than 50% were regulated as hazardous waste.

Alternatives for radioactive methods. Chemiluminescent reagents have been successfully developed as alternatives to radioactive materials in many research procedures (*149*) Use of these alternatives has been encouraged at NIH and other facilities. This has resulted in significant reductions in both procurement and disposal of radioactive materials.

Use of microscale techniques. Probably the most profound changes in waste generation that will occur in the near future will not result from intentional pollution prevention efforts; they will be a beneficial outcome of changes in research technology. Knapp et al. (*217*) referred to the paradigm shift that is now occurring in experimental techniques.

> In an analogous movement to that experienced by information technology, miniaturization and process integration are being implemented to revolutionize the way biochemical and chemical information is acquired.

Process enhancements and automation of research procedures are now rapidly reducing the size of equipment and volumes of reagents necessary to conduct sequencing, assays, and other common laboratory procedures. It may soon be possible to conduct many, if not most, of the common research procedures that once required liters of reagents and the space of a full laboratory on a microscopic scale. This has the potential to greatly reduce the use of chemical reagents and generation of hazardous wastes. For example, the amount of material required for experiments involved in the drug discovery process will be reduced to 1/1000 of the volumes currently required by the use of these "laboratories on a chip" (*218*).

Recommendations

The committee identified several areas where action is needed to improve management of wastes in research facilities.

Improve regulatory framework. Continue efforts to reinvent the regulatory framework governing waste minimization and management with the goals of enhancing environmental protection and eliminating regulations that impose significant burdens on the research mission without commensurate environmental benefits.

Expand training efforts. Incorporate subject matter pertaining to source reduction, waste minimization, and management into training programs for investigators, medical students, health care providers, procurement officers, and facility support personnel.

Incorporate design elements for pollution prevention into items used and developed by research. Ensure that pollution prevention and waste minimization objectives are considered in the research, design, development, selection, and use of all reagents, supplies, equipment, and procedures used in biomedical research. The same objectives should be applied to the products of biomedical research—all items used in the provision of healthcare.

Establish an information clearinghouse. Improve mechanisms for the transfer of current information on waste minimization and technology among all stakeholders—investigators, facility support personnel, regulatory agencies, and the public. The Pollution Prevention and Energy Efficiency Clearinghouse for Biomedical Research Facilities (*219*) proposed by this conference addresses this need.

Improve drug disposal. Give higher priority to research on the potential public health and environmental impacts of wastes containing drugs and their residues and on methods to mitigate these impacts.

Conclusion

The general conclusion reached by this committee responds to the primary concern raised by the conveners of this conference: there is no evidence to suggest that the anticipated increases in biomedical research will significantly increase generation of wastes or have adverse impacts the general environment. This conclusion assumes the positive, countervailing trends of enhanced pollution prevention efforts by facilities and reductions in waste generation resulting from improvements in research methods will continue.

References and Notes

1. Marwick C. Medical facilities to focus on cleaner environment. J Am Med Assn 280(6):501–502 (1998).
2. Grupenhoff JT. The environment and biomedical research. Environ Health Perspect 106:580–581 (1998).
3. National Association of Physicians for the Environment. Committee on Minimization and Management of Wastes from Biomedical Research. Available: *http://www.napenet.org/con99com.html#com5* [cited 8 December 2000].
4. Biennial Report. 40 C.F.R. 262.41 (1999).
5. U.S. EPA. Problems associated with management of hazardous wastes from educational institutions. Draft report prepared for U.S. EPA by ICF Inc. Washington, DC:U.S. Environmental Protection Agency, 1987.
6. California Environmental Protection Agency. Report to Cal/EPA Department of Toxic Substances Control. Recommendations of the Laboratory Regulatory Reform Task Force. Sacramento, CA: California Environmental Protection Agency, 1995.
7. U.S. EPA. Medical waste characterization. Report prepared for U.S. EPA by Energy and Environmental Research Corporation. Irvine, CA:Environmental Research Corporation, 1991.
8. Rutala WA, Mayhill CG. SHEA Position Paper: medical waste. Infect Cont and Hosp Epidemiol 13:38–48 (1992).
9. OTA. Partnerships under Pressure: Managing Low-Level Radioactive Waste. OTA-0-426. Washington, DC:U.S. Congress, 1989.
10. U.S. NRC. National Profile on Commercially Generated low-level Mixed Waste. NUREG/CR/CR-5938, Springfield, Virginia: National Technical Information Service, 1991.
11. Brainard J. EPA offices push colleges to comply with environmental regulations. Chron Higher Edu XLV(44):A32 (1999).
12. U.S. EPA. Higher Education on EPA Check List. Press Release dated May 25, 1999 (Revised June 4, 1999). Available: *http://yosemite.epa.gov/r3/press.nsf/7f3f954af9cce39b882563fd0063a09c/423561a2bc11c2b085256786005e5095?OpenDocument* [cited 8 December 2000].
13. Solid Waste Management Act of 1965. Public Law 89-272, 1965.
14. Resource Conservation and Recovery Act of 1976. Public Law 94-580 and subsequent amendments, 1976.
15. Pollution Prevention Act of 1990. Public Law 101-508, 1990.
16. Clinton WJ. Executive Order 13148 of April 21, 2000. Greening of the Government Through Environmental Leadership. Fed Reg 65(81):24595–24606 (2000).
17. U.S. EPA. Waste Minimization Opportunity Assessment Manual. EPA/625/7-88/003. Cincinnati, OH:U.S. Environmental Protection Agency, 1988.
18. U.S. EPA. Environmental Management Guide for Small Laboratories. EPA 233-B-98-001. Washington, DC:U.S. Environmental Protection Agency, 1998.
19. Wagner KD, ed. Environmental Management in Health Care Facilities. Philadelphia:W.B. Saunders, 1998.
20. Reinhardt PA, Leigh LK, Ashbrook PC, eds. Pollution Prevention and Waste Minimization in Laboratories. Boca Raton, FL:CRC Press, 1996.
21. ACS Task Force on Laboratory Waste Management. Laboratory Waste Management. A Guidebook. Washington, DC:American Chemical Society, 1994.
22. U.S. Department of Transportation. Hazardous materials: Revision to standards for infectious substances and genetically modified microorganisms. Fed Reg 63:46844–46859 (1998).
23. Wagner KD. Defining and characterizing the waste stream of healthcare facilities. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;9–17.
24. National Institutes of Health. NIH Guidelines. Recombinant DNA and Gene Transfer. Available: *http://www4.od.nih.gov/OBA/guidelines.html* [cited 11 April 2000].
25. Medical Waste Tracking Act of 1988. Public Law 100-582. 1988.
26. U.S. EPA. Frequently Asked Questions. Environmental Protection Agency Medical Waste Home Page. Available: *http://www.epa.gov/epaoswer/other/medical/mwfaqs.htm* [cited 20 July 2000].
27. ASTDR. The Public Health Implications of Medical Waste. A Report to Congress by the US Agency for Toxic Substances and Disease Registry. Washington, DC:Department of Health and Human Services, 1990.
28. CDC/NIH. Biosafety in Microbiological and Biomedical Laboratories. 4th ed. HHS (CDC) 93-8395. U.S. Centers for Disease Control and National Institutes of Health. Washington, DC:U.S. Government Printing Office, 1999.
29. Zaki AN, Campbell JR. Infectious waste management and laboratory design criteria. Am Ind Hyg Assoc J 8(11):800–808 (1997).
30. Rutala W, Odette R, Samsa G. Management of infectious waste by US hospitals. JAMA 262(12):1635–1640 (1989).
31. Collins CH, Kennedy DA. The microbiological hazards of municipal and clinical wastes. J Bacteriol 73:1–6 (1992).
32. Seeker WR. Medical waste incineration. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998.
33. Federal Water Pollution Control Act. Public Law 92-500 (1972) and subsequent amendments including the Clean Water Act of 1977, 1977.
34. Garcia R. Effective cost-reduction strategies in the management of regulated medical waste. Am J Infect Control 27(2):165–175 (1999).
35. Glaser DJ. Personal communication, 1999.
36. English N. Reprocessing disposables: one strategy to balance cost reduction and quality patient care. Today's Surgical Nurse 18(4):23–26 (1996).
37. Czajkowski-Beckwith H, Rosenblatt WH. Reprocessing unused surgical supplies for use in developing countries. AORN J 63(1):236–238 (1996).
38. Anonymous. Appendix C. Reuse of healthcare supplies: organizations, programs and information. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;332–338.
39. Fisher BE. Dissolving medical waste. Environ Health Perspect 104 (7):708–710.
40. New Source Performance Standards and Emission Guidelines for Hospital/Medical/Infectious Waste Incinerators. 40 C.F.R. 60, Subparts Ce and Ec, 1999.
41. Clean Air Act. Public Law 80-159 and subsequent amendments (1955).
42. Clean Air Act Amendments of 1990. Public Law 101-549 (1990).
43. U.S. EPA. Environmental Protection Agency Medical Waste Home Page. Available: *http://www.epa.gov/epaoswer/other/medical/index.htm* [cited 20 July 2000].
44. Spurgin RA. Nonincineration treatment technologies. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;28–39.
45. Turnburg WL. Biohazardous Waste. New York:John Wiley & Sons, 1966.
46. Freeman DS, Siskind GH. Medical Waste Handbook. Federal and State Regulations. 1998 ed. New York:Clark Boardman Callaghan, 1997.
47. Anonymous. Appendix E. Technical assistance manual: state regulatory oversight of medical waste treatment technologies. A report of the State and Territorial Association on Alternate Treatment Technologies. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;342–387.
48. Brown P, Rau EH, Bacote AE, Johnson BK, Gibbs CJ Jr, Gajdusek DC. New studies on the heat resistance of hamster-adapted scrapie agent: threshold survival after ashing at 600°C suggests an inorganic template of replication. Proc Natl Acad Sci USA 97(7):3418–3421 (2000).
49. Taylor DM. Transmissible degenerative encephalopathies. In: Principles and Practice of Disinfection, Preservation, and Sterilization (Russell AD, Hugo WB, Ayliffe GAJ, eds). London:

Blackwell Science, 1998;222–236.
50. Taylor DM. Inactivation of prions by physical and chemical means. J Hosp Infect 43 (suppl):S69–S76 (1999).
51. Taylor DM. Inactivation of transmissible degenerative encephalopathy agents: a review. Vet J 159:10–17 (2000).
52. U.S. Centers for Disease Control. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus, and other bloodborne pathogens in healthcare setting. Morb Mortal Wkly Rep 37:377–382; 387–388 (1988).
53. U.S. EPA. Disposal Tips for Home Health Care. EPA 530-F-93-027A. Washington, DC:U.S. Environmental Protection Agency, 1993.
54. Grau MV. Deposit-refund systems: a solution to medical waste management. Environ Eng Sci 14(1):27–32 (1997).
55. U.S. EPA. Waste Reduction Resource Center. Available: *http://wrrc.p2pays.org* [cited 20 July 2000].
56. Gilpin RW, Glazer SA. Unpublished data, 1999.
57. Ornelas D, Hogrefe RH, Dapson RW, Dapson JC. CE Update – Pollution Prevention. I: The role of chemical substitution in pollution prevention programs. Lab Med 29(5):287–290 (1998).
58. Ornelas D, Hogrefe RH, Dapson RW, Dapson JC. CE Update – Pollution Prevention. II: The laboratory's role in reducing hazardous waste. Lab Med 29(6):356–359 (1998).
59. Anonymous. Appendix F. Hazardous waste. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;388–411.
60. U.S. EPA. Technical Environmental Impacts of Various Approaches for Regulating Small Volume Hazardous Waste Generators. Vol 1. Washington, DC:U.S. Environmental Protection Agency , 1979.
61. U.S. EPA. The Waste Minimization National Plan. Available: *http://www.epa.gov/epaoswer/hazwaste/minimize/natlplan.pdf* [cited 14 July 2000].
62. U.S. EPA. Notice of availability of draft RCRA waste minimization PBT chemical list. Fed Reg 63:60332–60343 (1998).
63. Rau EH. Personal communication, 1999.
64. Merkle S. Personal communication, 1999.
65. Weaner LE. Personal communication, 1999.
66. Borenstein N, Radzinski T. Unpublished data, 1999.
67. U.S. EPA. Facility Pollution Prevention Guide. EPA 600-R-92-088. Washington, DC:U.S. Environmental Protection Agency, 1992.
68. U.S. EPA. Guides to Pollution Prevention. Selected Hospital Waste Streams. EPA /625/7-90/009. Washington, DC:U.S. Environmental Protection Agency, 1994.
69. Clark P. Personal communication, 1999.
70. Parrent M. Personal communication, 1999.
71. Lunn G, Sansone EB. Destruction of Hazardous Chemicals in the Laboratory. New York:Wiley Interscience, 1990.
72. Armour MA. Hazardous Laboratory Chemicals Disposal Guide. 2nd ed. Boca Raton, FL:CRC Press, 1996.
73. Comprehensive Environmental Response Compensation and Liability Act of 1980. Public Law 96-510 and subsequent amendments (1980).
74. Hazardous Materials Transportation Act. Public Law 93-633 and subsequent amendments (1975).
75. Superfund Amendments and Reauthorization Act of 1986. Public Law 99-499 and subsequent amendments, 1986.
76. Toxic Substances Control Act. Public Law 94-469 and subsequent amendments, 1976.
77. Heinlen D. BGSU's orphan chemical recycling program. In: Proceedings of a Specialty Conference: Challenges and Innovations in Management of Hazardous Waste. VIP-52, 10-12 May 1995, Washington, DC. Pittsburgh, PA:Air and Waste Management Association, 1995;107–110.
78. Pinnizzotto N, Baker SJ. Chemical waste disposal and recycling in an academic medical center. Chem Health Saf 7(2):22–25 (2000).
79. O'Brien E. Will mercury manometers soon be obsolete? J Hum Hypertens 9(12):933–934 (1995).
80. Blumenthal I. Should we ban the mercury thermometer? Discussion paper. J Royal Soc Med 85:553–555 (1992).
81. Grim CE, Garcia J, Fong RJ. The health risks of removing mercury manometers from the hospital and clinic. Am J Hypertens 7(4 part 2):116A (1994).
82. Mangum BW, Wise JA. Standard Reference Materials: Description and Use of a Precision Thermometer for the Clinical Laboratory. SRM 934. Special Publ 260-113. Gaithersburg, MD:National Institute of Standards and Technology, 1990.
83. Silverman BG, Daley WR, Rubin JD. The use of infrared ear thermometers in pediatric and family practice offices. Public Health Rep 113:268–272 (1998).
84. Weiss ME, Pue AF, Smith J. Laboratory and hospital testing of new infrared tympanic thermometers. J Clin Eng 16(2):137–144 (1991).
85. Emergency Care Research Institute. Guidance article on infrared ear thermometers. Health Devices 20(11):431–436 (1991).
86. Erickson RS, Meyer LT. Accuracy of infrared ear thermometry and other temperature methods in adults. Am J Crit Care 3(1):40–54 (1994).
87. Pontious SL, Kennedy A, Chung KL, Burroughs TE, Libby LJ, Vogel DW. Accuracy and reliability of temperature measurement in the emergency department by instrument and site in children. Pediatr Nurs 20(1):58–63 (1994).
88. MWRA/MASCO Mercury Work Group. Available: *http://www.masco.org/mercury* [cited 14 August 2000].
89. Holmer AF. 354 New Weapons Are in Development for the War on Cancer. New Medicines in Development for Cancer.1999 Survey. Washington, DC:Pharmaceutical Research and Manufacturers of America, 1999.
90. Pharmaceutical Manufacturers Association. Drug Companies Add 39 New Treatments to Nation's Medicine Chest, Increase R&D Investment to $24 Billion. Available: *http://www.phrma.org/pdf/charts/nda98.pdf* [cited 6 September 1999].
91. Spilker BA. The Drug Development and Approval Process Available: *http://www.phrma.org/charts/approval.html* [cited 6 September 1999].
92. Physician's Desk Reference. 53rd ed. Montvale, NJ:Medical Economics Company, 1999.
93. Davidson AW. The disposal of pharmaceutical waste. J Royal Soc Health 109(3):110–111 (1989).
94. Discarded Commercial Chemical Products, Off-Specification Species, Container Residues and Spills Thereof. 40 C.F.R. 261.33 (1999).
95. Characteristic of Ignitability. 40 C.F.R. 261.21 (1999).
96. Hazardous Waste Management System—General. 40 C.F.R. 260 (1999).
97. Standards Applicable to Generators of Hazardous Waste. 40 C.F.R. 262 (1999).
98. Controlled Substances Act. Public Law 91-513 and subsequent amendments (1970).
99. U.S. DEA. Chemical Handler's Manual—An Informational Outline of the Chemical Diversion & Trafficking Act of 1988. 276–770. Washington, DC:U.S. Government Printing Office, 1990.
100. U.S. DEA. A Security Outline of the Controlled Substances Act of 1970. Washington, DC:U.S. Government Printing Office, 1991.
101. Chapter I—Drug Enforcement Administration, Department Of Justice. 21 C.F.R. 1300 to End (1998).
102. Chemical Diversion and Trafficking Act of 1988. Public Law 103-200 (1988).
103. Domestic Chemical Diversion Control Act of 1993. Public Law 103-200 (1993) and Public Law 103-322, title XXXIII, Sec. 330024(c), (d) (1994), (1993, 1994).
104. U.S. DEA. Notice of proposed rulemaking. Fed Reg 60(163): 43732–43735 (1995).
105. Vaccari PL, Tonat K, DeChristoforo R, Gallelli JF, Zimmerman PF. Disposal of antineoplastic wastes at the National Institutes of Health. Am J Hosp Pharm 41:87–93 (1984).
106. Kuspis DA, Krenzelok EP. What happens to expired medications? A survey of community medication disposal. Vet Hum Toxicol 38(1):48–49 (1996).
107. Halling-Sørensen B, Nielsen SN, Lanzky PF, Ingerslev F, Lützhøft HCH, Jørgensen SE. Occurrence, fate and effects of pharmaceutical substances in the environment: a review. Chemosphere 36(2):357–393 (1998).
108. Daughton CG, Ternes TA. Pharmaceuticals and personal care products in the envrionment: agents of subtle change. Environ Health Perspect 107(suppl 6):907–939 (1999).
109. Wiltsie J. Personal communication, 1999.
110. Khachatourians GG. Agricultural use of antibiotics and the evolution and transfer of antibiotic-resistant bacteria. CMAJ 159(9):1129–1136 (1998).
111. Hun T. Studies indicate drugs in water may come from effluent discharges. Water Environ Technol 10(7):17–22 (1998).
112. Hignite C, Azarnoff DL. Drugs and drug metabolites as environmental contaminants: chlorophenoxyisobutyrate and salicyclic acid in sewage water effluent. Life Sci 20:337–341 (1977).
113. Heberer T, Dünnbier U, Reilich C, Stan HJ. Detection of drugs and drug metabolites in ground water samples of a drinking water treatment plant. Fresenius Environ Bull 6:438–443 (1997).
114. Stumpf M, Ternes TA, Haberer K, Seel P, Baumann W. Determination of pharmaceutics in sewage plants and river water. Vom Wasser 86:291–303 (1996).
115. Buser HR, Muller MD. Occurrence of the pharmaceutical drug clofibric acid and the herbicide Mecoprop in various Swiss lakes and in the North Sea. Environ Sci Technol 32(1):188–192 (1998).
116. Steger-Hartmann T, Kummerer K, Hartmann A. Biological degradation of cyclophosphamide and its occurrence in sewage water. Ecotoxicol Environ Saf 36:174–179 (1997).
117. Stan HJ, Heberer T, Linderhägner M. Occurrence of clofibric acid in the aquatic system—Is the use in human medical care the source of the contamination of surface, ground and drinking water? Vom Wasser 83:57–58 (1994).
118. Fontaine TD, Hoadley AW. Transferable drug resistance associated with coliforms isolated from hospital and domestic sewage. Health Lab Sci 13(4):238–245 (1976).
119. Bell RB. Antibiotic resistance patterns of fecal coliforms isolated from domestic sewage before and after treatment in an aerobic lagoon. Can J Microbiol 24(7):886–888 (1978).
120. Bell JB, Elliott GE, Smith DW. Influence of sewage treatment and urbanization on selection of multiple resistance in fecal coliform populations. Appl Environ Microbiol 46(1):227–232 (1983).
121. Walter MV, Vennes JW. Occurrence of multiple antibiotic-resistant bacteria in domestic sewage and oxidation lagoons. Appl Environ Microbiol 50(4):930–933 (1985).
122. Valdivia E, Martin-Sánchez I, Quirantes R, Martínez-Bueno M, Gálvez A, Maqueda M. Incidence of antibiotic resistance and sex pheromone response among enterocci isolated from clinical human samples and from municipal wastewater. J Appl Bacteriol 81:538–544 (1996).
123. Parveen S, Murphree RL, Edmiston L, Kaspar CW, Portier KM, Tamplin MI. Association of multiple-antibiotic-resistance profiles with point and nonpoint sources of *Escherichia coli* in Apalachiocola Bay. Appl Environ Microbiol 63(7):2607–2612 (1997).
124. Guardabassi L, Petersen A, Olsen JE, Dalsgaard A. Antibiotic resistance in Acinetobacter spp. isolated from sewers receiving waste effluent from a hospital and a pharmaceutical plant. Appl Environ Microbiol 64 (9):3499–3502 (1998).
125. Richardson ML, Bowran MJ. The fate of pharmaceutical chemists in the aquatic environment. J Pharm Pharmacol 37:1–12 (1985).
126. Sanz JL, Rodriguez N, Amils R. The action of antibiotics on the anaerobic digestion process. Appl Microbiol Biotechnol 46: 587–592 (1996).
127. Coile R. Defining the future of health care delivery. Am Coll Physician Exec News 2(6):1–2 (1999).
128. Hartmann A, Alder AC, Koller T, Widmer RM. Identification of fluoroquinone antibiotics as the main source of umuC genotoxicity in native hospital wastewater. Environ Toxicol Chem 17(3): 377–382 (1998).
129. Aherne GW, Hardcastle A, Nield AH. Cytotoxic drugs and the aquatic environment: estimation of bleomycin in river and water samples. J Pharm Pharmacol 42(10):741–742 (1990).
130. Desbrow C, Routledge EJ, Brightly GC, Sumpter JP, Waldock M. Identification of estrogenic chemicals in STW effluent. 1: Chemical fractionation and in vitro biological screening. Environ Sci Technol 32(11):1549–1558 (1998).
131. Jobling S, Nolan M, Tyler CB, Brighten G, Sumpter JP. Widespread sexual disruption in wild fish. Environ Sci Technol 32:2498–2506 (1998).
132. Routledge EJ, Sheanan D, Desbrow C, Brighton GC, Waldock M, Sumpter JP. Identification of estrogenic chemicals in STW effluent. 2: In vivo responses in trout and roach. Environ Sci Technol 32 (11):1559–1565 (1998).
133. FDA. Guidance for Industry. Environmental Assessment of Human Drug and Biologics Applications. Food and Drug Administration. July 1998 CMC 6, Revision 1. Available: *http://www.fda.gov/cder/guidance/index.htm.* [cited 30 August 1999].
134. FDA. Rules and Regulations. National Environmental Policy Act; Revision of Policies and Procedures; Final Rule. Fed Reg 62(145):40569–40600 (1997).
135. FDA. Guidance for Industry. Content and Format of Investigational New Drug Applications (INDs) for Phase 1 Studies of Drugs, Including Well-Characterized, Therapeutic, Biotechnology-derived Products. Available: *http://www.fda.gov/cder/guidance/clin2.pdf* [cited 2 November 2000].
136. Alger A. Gilding the Lilly. Forbes. 164(23):402–406 (1999).
137. Anonymous. Project cuts waste by tailoring ordering, production, distribution. Clinical Center News. Bethesda, MD: National Institutes of Health, 1–2 November 1995.
138. National Institutes of Health Clinical Center. National Institutes of Health Clinical Center Hazardous Drug List. Available: *http://www.cc.nih.gov/nursing/hazdrlst.pdf* [cited 2 November 2000].
139. Turnberg WL. Antineoplastic and other hazardous drug waste management. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998; 9–17.
140. The Health Physics Society. Low-Level Radioactive Waste: Position Statement of the Health Physics Society. Updated July 1999. Available: *http://www.hps.org/documents/llrw.pdf* [cited 2 November 2000].

141. International Commission on Radiological Protection. Radiological Protection Policy for the Disposal of Radioactive Waste. ICRP Publ 77. New York:Pergamon Press, 1997.
142. U.S. DOE. Low-Level Radioactive Waste Management in Medical and Biomedical Research Institutions. DOE/LLW-13Th. Idaho Falls, ID:EG&G Idaho, Inc., 1987.
143. U.S. DOE. 1995 State-by-State Assessment of Low-Level Radioactive Wastes Received at Commercial Disposal Sites. DOE/LLW-237. Idaho Falls, ID:Lockheed Martin Idaho Technology Inc., 1996.
144. U.S. DOE. 1996 State-by-State Assessment of Low-Level Radioactive Wastes Received at Commercial Disposal Sites. DOE/LLW-243. Idaho Falls, ID:Lockheed Martin Idaho Technology Inc., 1997.
145. U.S. DOE. 1997 State-by-State Assessment of Low-Level Radioactive Wastes Received at Commercial Disposal Sites. DOE/LLW-247. Idaho Falls, ID:Lockheed Martin Idaho Technoloogy Inc., 1998.
146. Standards for Protection Against Radiation. 10 C.F.R. 20.2003 (1999).
147. NRC. An Evaluation of Exposure Pathways to Man from Disposal of Radioactive Materials Into Sanitary Sewer Systems. NUREG/CR-5814. Washington, DC:Nuclear Regulatory Commission, 1992.
148. GAO 1994. Action Needed to Control Radioactive Contamination at Sewage Treatment Plants. GAO/RCED-94-133. Washington, DC:U.S. General Accounting Office, 1994.
149. Party E, Gershey EL. A review of some available radioactive and non-radioactive substitutes for use in biomedical research. Health Phys 69(1):1–5 (1995).
150. U.S. DOE. Commercial Radioactive Waste Minimization Program Development Guidance. EGG-LLW-9525. Idaho Falls, ID:EG&G Idaho, Inc., 1991.
151. Smith GD, Vetter RJ. Low-level radioactive waste management. In: Environmental Management in Healthcare Facilities (Wagner K, ed). Philadelphia:W.B. Saunders, 1998;89–94.
152. Massé F. Radiation safety in a large academic program. In: Management and Administration of Radiation Safety Programs (Roessler C, ed). Madison, WI:Medical Physics Publishing, 1998;215–254.
153. Tripodes JG. Minimizing and managing low-level radioactive waste. Med Waste Anal 2(1):1,3–5 (1993).
154. Hamrick PE, Davidson WE, Velazquez KW, Watson JE, Monitoring of 35S in ash of incinerated waste. Health Phys 65(5):556–559 (1993).
155. Kaye GI, Methe BM, Weber PB. Low-level waste management in an academic medical center. In: Hospital Health Physics (Eichholz G, Shonka J, eds). Richland, WA:Research Enterprises, 1993;229–244.
156. Hamawy G. Freeze-drying as a potential means for waste handling of animal carcasses containing radioactive material. Health Phys 69(1):115–120 (1995).
157. Saito K, Miyatake H, Kobori H, Kurihara N. Pretreatment of animal wastes containing radioisotopes with dry-distillation. Health Phys 69(1):117–120 (1995).
158. U.S. GAO. States Are Not Developing Disposal Facilities. GAO/RCED-99-238. Washington, DC:U.S. General Accounting Office, 1999.
159. U.S. EPA. Joint NRC/EPA Sewage Sludge Radiological Survey: Survey Design and Test Site Results. Available: *http://www.epa.gov/radiation/tenorm/docs/sludgereport.htm* [cited 11 August 1999].
160. Woeh WJ, Hatami A, Holodny EI. Radioactive waste volume reduction in a university/hospital setting. In: Managing Radioactive and Mixed Wastes, Proceedings of the Twenty Seventh Mid-Year Topical Meeting of the Health Physics Society, 13-16 February 1994, Albany, New York. Albany, NY: Health Physics Society, 421–422;1994.
161. Ring J, Osborne F, Shapiro J, Johnson R. Radioactive waste management at a large university and medical research complex. Health Phys 65(2):193–199 (1993).
162. Party E, Gershey EL. Recommendations for radioactive waste reduction in biomedical/academic institutions. Health Phys 56(4):571–572 (1989).
163. U.S. DOE. Low-Level Radioactive Waste Management in Medical and Biomedical Research Institutions. DOE/LLW/-13Th. Idaho Falls, ID:EG&G Idaho, Inc., 1987.
164. U.S. DOE. National Low Level Waste Management Program. Available: *http://www.inel.gov/national/national.html* [cited 8 December 2000].
165. National Research Council. Prudent Practices in the Laboratory: Handling and Disposal of Chemicals. Washington, DC:National Academy Press, 1995.
166. U.S. DOE. Guidelines for Mixed Waste Minimization. DOE/LLW-144. Idaho Falls, ID:U.S. Department of Energy, 1992.
167. NIH. Mixed Waste Minimization Strategies: Guidance for Investigators. Bethesda, MD:National Institutes of Health, 1986.
168. U.S. EPA. Extension of the policy on enforcement of RCRA section 3004(j) storage prohibition at facilities generating mixed radioactive/hazardous waste. Fed Reg 63(215): 59989–59992 (1998).
169. Waste Characteristics. 10 C.F.R. 61.56 (a)(8) (1998).
170. Rau EH. Trends in management and minimization of biomedical mixed wastes at the National Institutes of Health. Technology: J Franklin Inst 334(A):397–419 (1997).
171. Rau EH. Personal communication, 1999.
172. 40 C.F.R. Part 266. Storage, treatment, transportation, and disposal of mixed waste; proposed rule. Fed Reg 64(223):63464–63501 (1999).
173. Hoerr DC, Weaner LE. A prototype high-temperature catalytic oxidation process for mixed waste in a pharmaceutical research laboratory. In: Proceedings of the 1995 International Incineration Conference, 8-12 May 1995, Bellvue, Washington (Barnow L, Dempsey C, Tripodes J, eds). Irvine, CA:University of California Press, 1995;505–508.
174. Carr S. Personal communication, 1999.
175. U.S. EPA. Characterization of Municipal Solid Waste in the United States: 1995 Update Executive Summary. EPA 530-S-96-001. Washington, DC:U.S. Environmental Protection Agency, 1996.
176. French H. Minimization of medical waste through total integrated waste management. Poster session and presentation at the National Leadership Conference: Biomedical Research and the Environment, 1-2 November 1999, National Institutes of Health, Bethesda, Maryland, 1999.
177. Ohio Environmental Protection Agency. Research and Educational Laboratory Waste Reduction. Available: *http://www.epa.state.oh.us/opp/fact16.html* [cited 2 November 2000].
178. Accumulation Time. 40 C.F.R. 262.34 (1999).
179. Personnel Training. 40 C.F.R. 265.16 (1999).
180. Hazardous Waste Operations and Emergency Response. 29 C.F.R. 1910.120 (1999).
181. Instructions to Workers. 10 C.F.R. 19.12 (1999).
182. Notifications and Reports to Individuals. 10 C.F.R. 19.13 (1999).
183. Hazard Communication. 29 C.F.R. 1910.1200 (1999).
184. Bloodborne Pathogens. 29 C.F.R. 1910.1030 (1999).
185. National Institute of Environmental Health Sciences. Minimum Criteria for Worker Health and Safety Training For Hazardous Waste Operations and Emergency Response. National Clearinghouse on Occupational and Environmental Health Workplace Health Fund. 22-24 March 1990, Washington, DC. Available: *http://204.177.120.20/wetp/clear/resource/mincrter.html* [cited 14 August 2000].
186. Training Requirements. 49 CFR 172.704 (1999).
187. National Institute of Environmental Health Sciences. HAZWOPER Training Utilizing Advanced Training Technologies. 20-21 April 1999, Estes Park, Colorado.
188. Duplechan L. Hazardous waste management. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders Company, 1998;57–78.
189. Emmerman J. Laboratory Waste Management. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998;100–115.
190. NIH. NIH Waste Disposal Guide. Bethesda, MD:National Institutes of Health, 1997.
191. NIH. NIH Guide to Waste Disposal. Available: *http://www.nih.gov/od/ors/ds/wastecal/guide.htm* [cited 7 August 2000].
192. NIH. Mixed Waste: A Major Issue in Biomedical Research (a video film). Bethesda, MD:National Institutes of Health, 1992.
193. NIH. Radiation Safety Refresher Training, Waste Minimization Review and Update (a video film). Bethesda, MD:National Institutes of Health, 1995.
194. Medical Waste Institute. Transportation of Regulated Waste Compliance Assistance Document. Washington, DC:Medical Waste Institute, 1999.
195. AORN. Association of Operating Room Nurses (AORN) recommended practices for environmental responsibility in the pactice setting. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders Company, 1998; 323–326.
196. JCAHO. JCAHO Standard for Hazardous Materials and Waste. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders Company, 1998; 463.
197. Spurgin R. Non-governmental agencies and their standards and guidance. In: Environmental Management in Health Care Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders, 1998; 330–332.
198. Adapted from: Priznar F. What Makes Labs Unique? Lab Saf Environ Manage 7(5):4 (1999).
199. Wawzyniecki S. (Regulatory) fear and loathing on a campus dispelled after a RCRA inspection. Chem Health Saf 6(2):8–10 (1999).
200. National Research Council. Prudent Practices for Disposal of Chemicals from Laboratories. Washington, DC:National Academy Press, 1983.
201. California Environmental Protection Agency. Report to Cal/EPA Department of Toxic Substances Control. Recommendations of the Laboratory Regulatory Reform Task Force. Sacramento, CA:California Environmental Protection Agency, 1995.
202. U.S. EPA. Laboratory Project XL. Available: *http://www.epa.gov/projectxl.nelabs/index.htm* [cited 8 December 2000].
203. Howard Hughes Medical Institute. 1999. Managing Hazardous Wastes in Academic Research Institutions. Available: *http://www.hhmi.org/science/labsafe/projects/hazwaste.html* [cited 8 December 2000].
204. NIH. NIH Initiative to Reduce Regulatory Burden: Identification of Issues and Potential Solutions. Available: *http://www.nih.gov/grants/policy/regulatoryburden/index.htm* [cited 21 July 1999].
205. California Assembly. Assembly Bill No. 966, Chapter 506. An act to amend sections 25123.5 and 2550.6, and to add sections 25143.14 and 25200.3.1 to the Health and Safety Code, relating to hazardous waste (1998).
206. Alexander HR, Cartlett DL, Fraker DL, Libutti SK. Regional treatment strategies for unresectable primary or metastatic cancer confined to the liver. PPO Updates 10:1–19 (1996).
207. Alexander HR Jr, Bartlett DL, Libutti SK. Isolated hepatic perfusion: a potentially effective treatment for patients with metastatic or primary cancers confined to the liver. Cancer J 4(1):1–11 (1998).
208. Alexander HR, Brown CK, Bartlett DL, Libutti SK, Figg WD, Turner E. Augmented capillary leak during isolated hepatic perfusion (IHP) occurs via tumor necrosis factor-independent mechanisms. Clin Cancer Res 4:2357–2362 (1998).
209. Alexander HR Jr, Bartlett DL, Libutti SK, Fraker DL, Moser T, Rosenberg SA. Isolated hepatic perfusion with tumor necrosis factor and melphalan for unresectable cancers confined to the liver. J Clin Oncol 16(4):1479–1489 (1998).
210. Susman E. Partial responses encourage doctors to continue isolated hepatic perfusion for patient with colorectal cancer mets to liver. Oncol Times 21(6):33–34 (1999).
211. Leonard KL, Reinhardt PA. A survey of laboratory waste management and minimization practices. In: Pollution Prevention and Waste Minimization in Laboratories (Reinhardt PA, Leonard KL, Ashbrook PC, eds). New York:CRC/Lewis Publishers, 1996, 15–30.
212. Wagner KD. The Emergence of Environmental Concerns for Healthcare Facilities. In: Environmental Management in Healthcare Facilities (Wagner KD, ed). Philadelphia:W.B. Saunders Company, 1998;1–7.
213. NIH. Report of the NIH committee on alternatives to radioactivity (NCAR) to the Deputy Director for Intramural Research. Bethesda, MD:National Institutes of Health, 1996.
214. Klein RC, Gershey EL. Biodegradable liquid scintillation counting cocktails. Health Phys 59(4):461–470 (1990).
215. Elliot J. Liquid scintillation sample analysis in microcentrifuge tubes. Health Phys 64(10):86–90 (1993).
216. Wonderly SW. Solid scintillation counting: a new technique for measuring radiolabeled compounds. Appl Radiat Isot 40(7):569–573 (1989).
217. Knapp MR, Sundberg S, Kopf-Sill A, Nagle R, Gallagher S, Chow C, Wada G, Nikiforov T, Cohen C, Parce JW. Laboratory on a chip: a new experimentation format. Am Lab 30(22):20–26 (1998).
218. Kniss R. Revolution of the drug discovery process using laboratory-on-a-chip technology. Am Lab 30(24):40–42 (1999).
219. Barker LF, Rau EH, Pfister EA, Calcagni J. Development of a pollution prevention and energy efficiency clearinghouse for biomedical research facilities. Environ Health Perspect 108(suppl 6):949–951 (2000).